Preliminary Draft Comments
by the
Clean Air Scientific Advisory Committee (CASAC)
Particulate Matter Review Panel
on the Peer Review of the
draft *Air Quality Criteria for Particulate Matter (Second External Review Draft)* (EPA 600/P-99/002bB)

Please Note: The comments in this document represent preliminary comments prepared by some of the CASAC Panelists during their initial review of the draft review document. Not all Panelists provided comments sufficiently in advance of the meeting to be included here. These comments may be changed at any time and to any degree by the individual authors based on discussions at the meeting on July 23-24, 2001, or as a result of other input received by the panelist during the review process. These draft comments should not be quoted or otherwise disseminated, nor should they be taken to represent the views of the Clean Air Scientific Advisory Committee or the Science Advisory Board.

These draft comments are being made available to acquaint interested observers with the range of preliminary views that have been prepared by the Panel. The formal views of the CASAC will be presented in a final written report to the EPA Administrator subsequent to the meeting (delivery date TBA). The final version of these draft comments will appear in that final report as an Appendix.

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Preliminary draft comments of CASAC Particulate Matter Review Panel - Please do not quote or take out of context.

Fred Miller, PhD

Chapter 6

General Comments:

The chapter in its current form represents an extensive review of the available literature from epidemiological studies on the effects of particulate matter. The organization of the chapter into the major subheadings is appropriate. As one reads the chapter, there is a tendency for the $PM_{2.5}$ effects to be discussed in great detail and for the conclusion to be drawn that $PM_{2.5}$ is of more concern than $PM_{10-2.5}$. However, as the chapter develops, studies are presented showing the potential for coarse particles to have an effect. The balance of this discussion should be examined in particular as it is brought forth to the synthesis chapter.

Throughout the document values of $PM_{2.5}$ and $PM_{10-2.5}$ are presented. However, the document fails to make clear when $PM_{2.5}$ is a derived measurement vs. a direct measurement. This is critically important for standard setting purposes as correlation analyses provide different weight of evidence on average values compared to direct measurement. To help the reader in evaluating the strengths of the different studies, under Study Description it would be of value to simply indicate if measurements on exposure levels are direct or derived measurements.

Specific Comments:

	p. 6-20	The Schwartz (2000c) study in the table reports a $PM_{2.5}$ mean of 15.6 mg/m^3. The study was conducted using data from 1979 1986. Were $PM_{2.5}$ measurements available in the late 1970s? How was the mean for $PM_{2.5}$ arrived at?
	p. 6-23	The entry for the Smith study under Results and Comments brings up the topic of threshold. No discussion of this study follows until page 6-247. It is not clear why the emphasis in the discussion of Table 6-1 should be restricted to multi-city studies, particularly when individual studies bring up topics that are important for standard setting such as the concept of threshold, the statistical averaging time, or additional potential sensitive subpopulations.
	p. 6-53	The figure presented here shows that 10 of 13 $PM_{2.5}$ studies and 4 of 13 coarse mode studies show statistical significance. While this gives greater emphasis to the importance of both the fine and the coarse mode for standard setting, the discussion in the text does not bring this point out as strongly as it should be. For example, in the section on crustal particle effects on page 6-56, the studies are discussed with a tendency for not showing an effect and little discussion is involved for the four studies that did demonstrate effects of coarse mode particles.
	p. 6-77, l. 8 26	The slant towards interpretation of $PM_{2.5}$ and relative dismissal of the importance of the coarse mode is continued in this section here on fine and coarse particle effects. The paragraph clearly comes across as there may be some PM coarse mode effects but they probably are specific in location and they may even be due to biogenetically-derived particles. In addition, the statements throughout the chapter reflect strong statements of $PM_{2.5}$ causing effects and then the statements around the coarse mode, i.e., PM_{10-25} use phraseology such as may also be important . This comes across to the reader as a bias of the authors relative to fine vs. coarse mode effects. This tone is

		continued on page 6-78, l. 2 4 where the statement is made that crustal particles do not appear overall to support associations with mortality in the source oriented evaluations. While clear recognition must be given that there are more studies demonstrating the importance of $PM_{2.5}$, the dismissal of coarse particles in the presence of positive studies is disconcerting, particularly given that much of the western part of the United States has PM_{10} dominated by the coarse mode fraction.
29	p. 6-84, Table 6-6	In the cardiopulmonary mortality column for the six cities original vs. the HEI reanalysis, a consistency of the point estimate is what one would expect. However, the much larger difference in the confidence limit bounds is surprising. It would be worth checking the entry in this table to ensure that a typographical error has not occurred.
30	p. 6-105, l. 11 26	The actuarial and statistical calculations presented based upon Brunekreef are hard to believe. The implication that the life span of persons exposed to and dying from air pollution is a reduction of more than 10 years, if true, would surely have been detected without the kind of sophisticated statistical analyses that are currently being required. In addition, what exactly is meant by implying that up through age 25 a loss of 1.31 years occurs for the entire population? Is this life span reduction? If so, actuarial numbers likely contradict this conclusion.
31	p. 6-107, l. 17	The conclusion from the Krewski et al. study that mortality may be associated with more than one component of the complex of ambient pollutants in urban areas bears emphasis in the synthesis chapter and is appropriately highlighted in various sections of the epidemiological discussions.
32	p. 6-107, l. 30	The mortality log hazard ratio increasing to 15 mg/m^3 and then being flat before continuing to increase again, while being a statistical model that appears to fit the data, has little biological motivation to support it (i.e., such a model makes little biological sense).
33	p. 6-108, l.8 13	The Krewski et al. study looking at the relative risk and incorporating time-dependent estimates is particularly important for the standard setting process. EPA must factor the temporal decline in PM that has been occurring in its assessment of the need for revisions of or new standards for particulate matter. This is particularly important with the various implementation strategies that have yet to take effect that are clearly leading to a reduction in overall pollution levels in this country.
34	p. 6-205, l. 10 19	A number of studies on long term effects from PM are cited as having been conducted in California but with inconsistent results. Yet the authors choose to describe the McConnell study as the most notable because it showed an increase that is similar to results reported by Dockery. Why is this study notable? It appears the authors have considered it such because it found effects when others didn t. This does not appear to be a balanced representation and discussion of the newly available studies.
35	p. 6-230, l.17 20	The nonlinear model for fine PM effects in the study by Smith et al. is of potential interest since a threshold between 20 25 mg/m^3 for $PM_{2.5}$ was seen in this study. Has the type of model presented by Smith et al. been applied in other data sets?
36	p. 6-247, l. 25	The summation of the Smith study relative to threshold selection and importance of fine vs. coarse is phrased as these results, if they in fact reflect reality, make it difficult to evaluate the relative role of different PM components One might interpret the authors use of the phrase if they in fact reflect reality as a bias for wanting to attribute one of the two modes as being more important. Alternatively, the sentence is an excellent summary of why the

PM issue is so entangled and difficult to separate on a causative basis for one mode vs. the other. In fact, such kinds of difficulties are precisely why the Agency must look carefully at standards for PM that encompass the full spectrum of potential effects in different locations.

Chapter 7: Dosimetry of Particulate Matter

General Comments:

Chapter 7 on the dosimetry of particulate matter primarily focuses on an update of new studies since the 1996 Criteria Document (CD). While the chapter provides a reasonable review of the available literature, the review is lacking in details in a number of areas. Given the importance of and reference to dosimetry considerations elsewhere in the document, the chapter should be strengthened with more specific presentations of some of the latest results.

The chapter fails to take advantage of a graphical representation of the more recent data. Such graphical representations covering susceptible subgroups in comparison to normal subjects would be of great value. The authors failed to report whether increases compared from one group to another are actually statistically significant or just represent general trends. Without showing the data and the standard deviations or error bars, the reader is left with a general uncertainty about the significance of any differences that are reported.

Section 7.5 on the comparisons of deposition and clearance patterns of particles administered by inhalation intratracheal instillation adds little to the chapter. This section, while accurate, is of little value for the risk assessment of particulate matter. There is no mention of the role that intratracheal administration can play in hazard identification and in mechanism of action studies. If this section is retained, clearer identification of the value of the animal toxicological studies using this method should be discussed. This is particularly important since many of the studies presented in Chapter 8 on animal toxicological results arise from intratracheal administration experiments. Section 7.5 should be reduced in size if it is retained.

Detailed tables or graphs contrasting deposition in children compared to adults should be presented in the chapter. Since arguments are made elsewhere in the CD about children being a potential susceptible population, dosimetric differences between children and adults need to be presented in greater detail than they currently are. The logic of having the only figure in the dosimetry chapter be one of total deposition is not apparent. While such data are of general interest, the types of effects and standard setting concerns focus on the major regions of the respiratory tract. Regional deposition should be presented and should incorporate recent research on different subpopulations and disease groups.

Specific Comments:

	p. 7-2, l. 16	The reference to information related to the phenomenon of particle overload is stretching the case for inclusion of this material. Clearly, there are no ambient exposures of particulate matter that approximate anything close to the exposure levels needed to induce overload of alveolar macrophage-mediated clearance that is the basis for this phenomenon in animals.
	p. 7-5, l. 7 11	The authors should clarify that the importance being described for various deposition mechanisms in respiratory tract regions applies to humans. The importance of some of these mechanisms differs on a relative sense for some and on an absolute sense for others when referring to particle deposition in animals.
	p. 7-6, l. 21 27	The cast studies with charged particles are not very relevant to real world

		ambient aerosols. If this material is retained, a better explanation of where these results might be applicable for potential real world exposures should be provided.
77	p. 7-7, l. 6 16	It is important in this paragraph to contrast inhalability in humans compared to inhalability of particles in animals. Otherwise the reader has no insight as to why this is an important concept to introduce and further has no reference for determining some of the relevance of concentrations used in animals when judging the potential for effects in humans.
78	p. 7-8, l. 1 7	Of value would have been to compare the recent results of Kim to those previously published by the GSF group for various combinations of tidal volumes and respiratory frequencies.
79	p. 7-10, l. 14 19	Since the study by Lenin used a fairly narrow size range (0.3 2.5 mm), the statements concerning particle size and flow rate and various breathing modes, while accurate, should be stated in such a way that the reader understands that these conclusions do not hold for a wider range of particle sizes.
80	p. 7-13, l. 24	The study by Kim and Fisher using sequential double bifurcation tube models, while yielding interesting results, should be put into perspective given that downstream flow affects deposition in the whole lung and is not necessarily approximated by sequential series of double bifurcation models.
81	p. 7-14. l. 26	The study by Venkataram and Kao 1999 used totally unrealistic breathing conditions in that they assumed breathing for 24 hours at conditions that are not physiologically sustainable. Only general trends can be inferred from their calculations as the quantitative values are not useful.
82	p. 7-15, l. 25	The paragraph beginning with this line should be reworked. The statements made in this paragraph are inconsistent with earlier statements of a decrease in deposition for particles with an initial diameter less than 0.5 mm and an increase in deposition with an initial diameter greater than 0.5 mm.
83	p. 7-17, l. 21	A gender difference of about 15% at rest for particle deposition is stated for the studies of Kim et al. Was the 15% change statistically significant? Without this information the reader can t really interpret the significance of the findings.
84	p. 7-19, l. 18 30	The way the Bennett et al. study is presented the reader cannot really judge the importance of the reported data. on ET deposition. ET deposition as a percentage of total respiratory tract deposition is the basis for making statements about differences in percentages. While these differences are statistically different, they are restricted to 4.5 mm particles since this was the only particle size Bennett et al. studied. However, the statement in the CD about the trend for ET deposition tending to increase as age decreased is not a statistically significant observation. The contention that the deposition seen in the cystic fibrosis children studied by Bennett et al. likely reflects what one would expect in normal children is suspect. The argument presented by Bennett et al is not convincing in that just because lung deposition is expected to be increased in cystic fibrosis children does not infer that ET deposition would tend to be decreased in these kids. Since ET deposition is upstream relative to lung deposition, one can not infer the negative (i.e., increased lung deposition does not confer that ET deposition should be decreased in cystic fibrotic children compared to normal children).
85	p. 7-20, l. 12 15	Again, are the differences reported statistically significant?
86	p. 7-24, l. 3 10	Recent results published by Asgharian et al. (Aerosol Sci. 32, 817 832, 2001) also support the influence of lung size on the retention of particles in the tracheobronchial region for periods longer than 24 hours after deposition.
87	p. 7-27, l.10 22	The way the paragraph comes across in describing the results in Musante and Martonen to infer that the rat may not be a good model for the resting human

		masks the fact that one has to account for differences in doing interspecies extrapolations. To make the argument that a greater activity level yields a more similar distribution of dose on a regional basis does not necessarily imply that this mode would be better since, for example, the distribution of types of cells within the respiratory tract differ by airway generation between the rat and the human. This paragraph could be expanded upon to point out some of the differences that must be taken into account when extrapolating between species.
88	p. 7-29, l. 20	Rather than starting the sentence with the phrase for the most part , the author should indicate that for hygroscopic particles and liquid droplets, clearance mechanisms are different compared to poorly soluble particles.
89	p. 7-34, l. 25	Asgharian et al. (Aerosol Sci. 32, 817 832, 2001) recently showed that it is not necessary to invoke a slow- and a fast-phase for tracheobronchial clearance to have particles retained in the TB region longer than 24 hours. Intersubject variability in retained mass arising from the periphery of the TB based upon lungs with variable number of airways can explain the experimental observations while still fitting a single compartment clearance model.
90	p. 7-40, l. 4 7	References should be supplied to support the statement made in this paragraph.
91	p. 7-40, l. 14	Physical activity is not really a biological factor in comparison to the other subsections covering age, gender, and the like. Why not simply entitle Section 7.3.4 Factors Modulating Clearance?
92	p. 7-49, l. 20	In an effort to make the chapter brief, the authors have indicated that additional work on modeling deposition in animals has been published but that it merely expands on work and approaches already noted in the 1996 PM Criteria Document. The text would leave most readers with the idea that the additional work is not of value. Since the work of Hoffman et al. (2000) is described on the next page, surely the inference is not that this is the only work that has made additional contributions. Some of the features and some of the additional references should be included here to provide a perspective on what the thrust of the additional work has been. To merely say that it has expanded upon previous work is not sufficient. For example, recent experimental and modeling work on particle deposition with pulsating flow in a rat nasal mold by Asgharian et al. (Inhal. Toxicol. 13: 577-588, 2001) demonstrates that deposition efficiencies for pulsating flows are markedly higher than for steady flows.
93	p. 7-50, l. 7 12	The statement that models have not been adapted to examine low level exposures to particles of low toxicity and poor solubility is incorrect. Koch and Stöber (Inhal. Toxicol. 13: 129-148, 2001) published a pulmonary retention model that accounts for dissolution and macrophage-mediated removal of deposited polydisperse particles. Their model and the results arising therefrom should be discussed.
94	p. 7-50, l. 13	The Asgharian et al. reference has the incorrect year. 2000 is cited in the text, but the correct year is 1995.
95	p. 7-51, Section	There does not appear to be a compelling reason that a separate section should
96	7.6.2	be devoted to models that estimate retained dose. Estimation of retained dose is a natural extension of models that handle both deposition and clearance processes. The material discussed in this section should be integrated into the clearance discussion because the various topics that are presented form the basis of clearance models of varying degrees of sophistication depending upon how much is known about the biological process.
97	p. 7-52, l. 25	Strike recently, from the sentence describing the work of Nikula et al. (1997). The year 1997 is no longer recent compared to 2001.
98	p. 7-52, l. 22 31	This paragraph lacks a punch line. While interspecies differences in interstitial

translocation and retention of particles is established, the statement is made that these interspecies differences may not occur at low levels of exposure. What is the justification for this statement? Are there any references to support this conclusion?

Chapter 8: Toxicology of Particulate Matter

General Comments:

Since toxicological studies are presented for both animals and humans, the title of this chapter should reflect such. In the past, toxicology has been usually restricted for description of animal results. This chapter provides a reasonable summation of the findings of studies that have been conducted since the 1996 Criteria Document. Unfortunately, as reflected in the summary, the biological plausibility of various constituents and mechanisms of action for effects are still not clearly established.

Section 8.5 of the chapter is labeled as Mechanisms of PM Toxicity from In Vitro Exposures. In actuality much of the material presented is simply effects from in vitro studies and really not insightful on mechanisms of actions of PM. The organization of the chapter in this way begs the question as to whether any mechanistic insights have been or can be gained from in vivo studies. Since I do not think that is the intent, cross referencing to in vivo and inhalation studies that correlate types of responses or effects seen with those in in vitro studies should be made whenever possible.

Specific Comments:

	p. 8-9, l. 19 22	The statement is made that it is not clear that the total dose of iron oxide delivered acutely to the lungs of human subjects would be relevant to deposition of iron given its concentration in ambient environment. A much stronger statement can be made. Just consider a minute ventilation of 15 liters per minute. Doing the calculations for 1 mg/m^3 in the air, the amount instilled bears no semblance to reality of what could be deposited in any reasonable acute exposure to these levels (e.g., assuming no clearance of particles and 100 % deposition, more than 7 months would be needed to deposit 5 mg of the iron oxide particles in the lung since only about 20 mg would be deposited in a day).
	p. 8-16	The concentration stated in the table for the Madden et al. study should be 1000 mg in 0.5 ml.
	p. 8-17	For the Watkinson et al. study, what were the nose-only inhalation concentrations?
	p. 8-18, Table 8-5	Given the low exposure of 10 mg/m^3 for 4 hours in the Ohtsuka et al. study, this paper warrants expanded discussion in the text.
	p. 8-24	The symbol for the geometric standard deviation is not as it appears in the table but rather should be the Greek symbol s. The same statement can be made for Table 8-7.
	p. 8-28, Table 8-7	This reviewer finds it of great interest that intertracheal instillation of ROFA in the Watkinson et al. study showed effects but inhalation of 15 mg/m^3 six hours per day for three days of the same compound showed no effects.
	p. 8-29, l. 11 20	In the Killingsworth et al. Studies using monocrotaline-MCT, mortality and changes in MIP-2 were noted. What human condition does this model mimic?
	p. 8-32, l. 6 19	This paragraph comes across as if the Godleski et al. HEI Report is considered peer reviewed and the study by Muggenberg et al. appearing in an *Inhalation Toxicology* Supplement from the PM 2000 Meeting is not peer reviewed. The fact that these studies differed in their findings is what should be emphasized because Godleski used concentrated ambient particles and Muggenberg used

		high concentrations of ROFA. If EPA has criteria for what the agency considers peer reviewed versus not peer reviewed, these criteria should be so stated and applied uniformly throughout the Criteria Document.
127	p. 8-31, l. 18 19	The statement is made that the different findings between the dog studies illustrate the difficulties in extrapolating animal toxicological data to human health effects. The sentence falls short in that it fails to note that lack of understanding of mechanism of action is the primary problem with extrapolating animal results that are disparate in nature to humans.
128	p. 8-33, l. 6 9	The results from the Gordon et al. study are interpreted in this paragraph to suggest that day-to-day changes in particle composition may play an important role in the systemic effects of inhaled particles. This is an overinterpretation of
129	p. 8 34, l. 4 14	In addition to the potential mechanisms discussed in this paragraph, the role of endothelins should be mentioned. Vincent et al. (Inhalation Toxicology of Ambient Particulate Matter: Acute Cardiovascular Effects of Resuspended EHC-93 Urban Particles in Wistar Rats. Final Report to the Health Effects Institute for the Collaborative Study 98-32, In Press, 2001) have shown that particles can affect endothelin 1 and 3 more than 30 hours post exposure.
130	p. 8-37, l.10	Replace the word although with the word after.
131	p. 8-41, l. 18	Broad statements such as what Nell et al. made in their article on suggesting that the rise in the U.S. prevalence rate for allergic rhinitis may be related to increased diesel emissions in addition to other combustion sources is highly speculative. Anyone can suggest a material is the culpritive agent for an effect but the emphasis in a criteria document ought to be on the proof for such relationships based upon experimental data.
132	p. 8-46, l. 13	The astronomically high carbon black exposure level used by Jakab produced no effect on susceptibility to bacterial infection in contrast to high exposure studies with titanium dioxide. Comparing such results implies that a particle is not a particle and that composition or the nature of the particle is important for the effects on the host. The Criteria Document does not put as much emphasis on pointing out concepts such as this as what might be appropriate.
133	p. 8-61, l. 3	Round 11.9-fold to 12-fold. Such rounding is undoubtedly more in accord with the accuracy of the data.
134	p. 8-62, l. 3	The concept discussed here that a combination of several components rather than a single metal in PM is likely responsible for cellular effects is worth bringing forward as one of the major conclusions that can be gained from examining the toxicological data on PM.
135	p. 8-67, l. 4	The Lee et al. studies described here involved sulfuric acid aerosol concentrations so high as to make the results of little value to the discussion of ambient PM effects. The paragraph describing this study should be deleted.
136	p. 8-70, l. 3	Insert the word to after the word shown.
137	p. 8-71, l. 5 24	Perhaps the authors of this chapter would comment on the paradoxical outcome of results found by Churg contrasting fine and ultrafine particles. Is the rat tracheal explant model a reasonable one for making the kinds of comparisons that were done by Churg et al.?

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139 ## Arthur C. Upton, MD

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141 Transmitted herewith, as requested, are my comments on chapters 6 and 9 of the draft citeria
142 document on PM. In general, I consider these chapters to be excellent, and I have no substantive
143 changes to suggest on either of them. Both chapters do, however, need careful editing to deal

with such problems as the following:
Pages 6-6, line 23 and 6-39, line 1: "most all" is ambiguous.
Page 6-267, lines 19-20: grammatically incorrect (words missing?).
Page 9-7, line 10: "this chapter and" should be deleted.
Page 9-8, last line: the reference to "Wilson and Suh" is missing from the bibliography, as are many of the other references cited elsewhere in the chapter.
Page 9-16, line 3: the second "is" should be changed to "are".

In addition to editorial corrections such as those noted above, the document needs a glossary to define the many technical terms and acronyms that are used in these and other chapters.

Barbara Zielinska, PhD

Review of Air Quality Criteria for Particulate Matter, Chapter 2: Physics, Chemistry, and Measurement of Particulate Matter

In my opinion, this chapter requires more work. At present, the chapter makes the impression on the reader that it was written by several independent authors, without any attempt to integrate it into one consistent document. Following are the specific examples:

1. On page 2-47, line 19-21 (Section 2.2.3), the authors state discussing the experiments with two quartz fiber filters deployed in series in order to examine the artifacts connected with SVOC partitioning: "Unless the individual compounds are identified, the investigator does not know what to do with the loading value on the second filter (i.e. to add or subtract from the first filter loading value)". I agree with this statement - moreover, even if the individual compounds were identified on back-up filter, the decision concerning adding or subtracting back-up filter loading would not be straightforward. However, the authors discuss subsequently in detail (page 2-51 to 2-62) in several places throughout the Section 2.2.3 several experiments with Teflon-quartz or quartz-quartz back-up filters that produced conflicting results. The references of Turpin et al., 2000, and Kirchsteller et al, 2000, are discussed on p. 2-52 – 2-53 and again on p. 2-61 – 2-62 (in addition, the reference of Turpin et al., 2000, is missing). This would be confusing to the reader who is not very familiar with the problem of positive and negative sampling artifacts. It would be desirable to organize the discussion in more consistent manner, shorten it significantly, and not scatter it throughout the whole Section 2.2.3

2. There are repetitions of the same statements throughout the chapter. For example, the discussion of sulfate and nitrate in western and eastern U.S. on page 2-21 (line 12-22) is repeated on page 2-51 (line 1-7).

3The discussion of the various denuder techniques and their limitations (Sections 2.2.3.2 and 2.2.3.3) is certainly important, especially since the popularity of these techniques has increased greatly recently. The selection of the correct denuder type, its dimensions, flow rate, etc., greatly influence the results and incorrect conclusions could be drawn if the user is not familiar with the denuder technique. It would be desirable if authors put more emphasis on discussing these factors and organize them in more logical manner (instead of the extensive discussion of the front-back-up filters collection methods, which produce doubtful results anyway).

Some statements or opinions express by authors are not accurate, for example:

1. Page 2-19, line 18-19: "…some primary organic compounds … are found…in the fine particle mode." As a matter of fact, most of the combustion-generated organic compounds are found in the fine particle mode.
2. Page 2-24, line 13: "…adsorption of organic gases…(e.g. polycyclic aromatic hydrocarbons)". Only 2 ring PAH are gaseous at ambient temperature, with 3 and 4 ring PAH distributed between the gas- and particle-phases.
3. Page 2-53, line 3-12: this discussion is impossible to follow, is there part of the sentence missing?
4. The PC-BOSS and RAMS denuders are discussed extensively throughout the chapter (page 2-55, 2-58, 2-89, 2-103, 2-105). However, both devices use a virtual impactor upstream of the denuder that removes not only a majority of the gases from the aerosol flow, but also particles smaller than 0.1 um. Thus, the gas-particle distribution is changed even before the aerosol enters the denuder! In addition, particulate OC estimates have to be corrected for particle losses in the inlet of 46 to 48%. Is this 46 to 48% factor independent of temperature, pressure and other factors? How accurate are the measurements, taking into account these corrections? It would be desirable if authors discuss the limitations of these denuders as well as put the results obtained with these devices in proper perspective.
5. Page 2-95: The discussion of the commercially available automated carbon analyzer seems to be a little premature in this document, since no comparison data with other established techniques is available yet. There is no clear understanding what the instrument really measures in comparison with TOR and TOT techniques.
6. For completeness, a newly developed continuous photoacoustic technique for black carbon measurement should be included in Section 2.2.5. The technique and its applications are described by Moosmuller et al. (1998) and Arnott et al. (1999; 2000).
7. Page 2-103, line 18-23: One has to be careful when expressing the opinion that the denuder technique is an improvement over the filter/adsorbent collection method. It should be followed by the caveat that this is not an "out of the shelf" technique, it is not straightforward and requires thorough understanding by the user. If not used properly, it is subject to numerous artifacts and may lead to erroneous conclusions. Also, one doesn't have to use a charcoal impregnated glass-fiber filter for SVOC collection (especially that it is not readily available commercially); other solid adsorbents (such as PUF/XAD plugs) are used as well.

The minor problems that require corrections are as follows:

1. Page 2-10, line 4-5: missing word, "the term ultrafine", "the term nanoparticle"
2. Page 2-13, line 13: prior to 1987
3. Page 2-20, line 22: "…or on or in.."?
4. Page 2-21, line 7: "in" before SO4 not necessary
5. Page 2-25, line 1: "are" is missing
6. Page 2-33, line 29: what is "PNA organic compounds"?
7. Page 2-56, line 19-21: an awkward sentence, instead of which method?
8. Page 2-57, line 23-25: this sentence is a repetition of the line 16-17
9. Page 2-62, line 15: absorbent?
10. Page 2-73, line 19: The instrument operated by the Desert Research Institute was not a "high-volume carbon sampler", but the medium-volume (113 L/min flow rate) fine

particles ($PM_{2.5}$) and semi-volatile organic compounds (i.e. filter followed by a solid adsorbent) sampler.

11. Page 2-77, line 13-14: an awkward sentence, I'm not sure what it means
12. Page 2-83, line 21-27: either "it is important" or "its importance"
13. Page 2-91, line 8: remove "because"
14. Page 2-105, line 23-25: not all ATOFMS instrument can measure particles ranging in size from 10 nm to 2 um (see page 2-94).

There are several missing references, mostly recent ones (Turpin et al., 2000; Casimiro et al., 2001) but also older, such as Turpin et al., 1991. I didn't check them all – it would be desirable if authors make sure that the references are in order.

References:

Arnott et al., 1999: Atmospheric Environment, 33, 2845-2852;
Arnott et al., 2000: Rev. Sci. Instrum., 71, 4545-4552;
Moosmüller et al., 1998: J. Geophys. Res., 103, 28,149 – 28,157

Review of Air Quality Criteria for Particulate Matter, Chapter 3: Concentrations, Sources, and Emissions of Atmospheric Particulate Matter

I would recommend several minor revisions for this chapter, as follows:

1. Page 3-5, line 1-3: Figure 3-2 shows that although the nationwide PM_{10} concentration trend shows the clear decline from 1989 to 1995, it seems to level-out for the last 3 years, especially for urban-suburban sites.
2. Page 3-6, Figure 3-3 is not clear. The reader may have troubles with assigning the EPA regions to the graphs.
3. Page 3-22, line 4: the main reason of heated inlets in continuous PM mass measurement instruments is to remove water (as discussed in Chapter 2), so the removal of water is not a sampling artifact.
4. Page 3-26, line 26-30, the discussion of Table 3-3: it is not apparent from the data presented in this table that water and cations associated with sulfate are the most abundant species in Philadelphia. Also, sulfate concentrations is not listed, just the total sulfur.
5. Page 3-28, line 7-9: not only trace metals concentrations are highly uncertain; Al shows very high uncertainty as well.
6. Page 3-30, line 18 to the end of the paragraph, the discussion of Table 3-5. The selection of marker species for individual source categories seems to influence greatly the results. In particular, Pb, Br and Mn as the only tracers do not seem to adequately represent motor vehicle emissions.
7. Page 3-35, Table 3-7: EC sources for anthropogenic PM>2.5 include tire and asphalt wear as well.
8. Page 3-42, line 13-15. Table 3-1 doesn't show that water, sulfate and cations associated with sulfate are the major components of PM in the eastern U.S. Also, the newer studies listed in Table 3-8 showed that not only diesel but also gasoline vehicle exhausts are important sources of PM.
9. Page 3-45, line 8-10: an awkward sentence
10. Page 3-45, line 30: 1998, not 1988
11. Page 3-46, line 5-6: "However… but…"?

12. Figure 3-23, page 3-50: the figure caption says "… principal source categories for nonfugitive dust sources…", but the figure shows 44.2% of fugitive dust contribution.
13. Page 3-56, line 11-13: This is not a valid argument, since $PM_{2.5}$ which are discussed here, have longer residence time.
14. Page 3-56, line 28-30: an awkward sentence
15. Page 3-57 and 3-58, line 29-31 and 1-3: please clarify
16. Page 3-59, line 7-9: the discussion on page 3-55 and 3-56 states that the reasons for this apparent discrepancy between emission inventory and receptor modeling results are not clear.
17. Page 3-59, line 21: what PM2.5PM10 refers to?
18. Appendix 3A: Table 3A-2 should include some data from more recent Northern Front Range Air Quality Study (NFRAQS), carried out in winter 1997. Ambient data are presented in volume A (Chow et al., 1998) of the final report (Watson et al., 1998) and are available on the web (http://www.nfraqs.colostate.edu/index2.html)
19. Appendix 3A, Table 3A-2: Are organic compound concentrations really in ngC/m^3 (C = carbon) or rather in ng/m^3?
20. Appendix 3B, page 3B-12, line 13-15: fuel type?
21. Page 3B-13, line 1-10: are "diesels" mentioned here light- or heavy-duty vehicles?
22. Page 3B-18, line 1-17: PAH were also reported in volume B (Zielinska et al., 1998) of the NFRAQS final report (Watson et al., 1998)
23. Page 3B-18, line 7-10: at atmospheric conditions, PAH with mw 228 (BaA, chrysene and triphenylene) are predominantly particle-associated, with only traces of these PAH in the gas-phase (see, for example, Arey et al., 1987).

References:

Arey et al., 1987: Atmospheric Environment, 21, 1437-1444 (page 1439)

Joe L. Mauderly, DVM

Chapter 7: Dosimetry of Particulate Matter

General Comments:

This chapter covers a reasonable range of topics, but needs some editing. There are several places where terms are used incorrectly, or where uncommon terms are not defined.

Throughout the chapter, it should be stated whether the exposures of humans were nasal, oral, or both. The difference affects deposition, as the author notes, and the results from individual studies can't be placed in context by the reader without the information.

Throughout the chapter, it should be stated whether the models and their predictions have been validated by comparison of results to those from actual measurements. More models have not been validated than have. This is an important point for the reader to understand.

The chapter could benefit from the addition of a few more figures and tables showing comparative data that illustrate the points being made. A reader well-informed on deposition/retention issues can understand the points being made, but many readers will have

difficulty envisioning the relationships described. A simple graph of particle size vs. regional and total deposition taken from any of the several sources cited would help. Figure 7-1 is not inappropriate, but it falls unnecessarily short of illustrating both total and regional deposition. A table listing some representative values for comparative (between species) amounts of deposited and retained PM of a few discrete sizes would also help. Other than the figure on Page 7-8 and the flurry on pages 7-30-31, the chapter makes no use of tabular or visual material to illustrate key points.

Specific comments:

P 7-3, L 12: Don't confuse "aerosols" with "particles". It's the particles that have a polydisperse size distribution. The "size" of an aerosol is the size of its container.

P 7-6, L 1: All deposition is "by physical contact". What we are talking about are the mechanisms that cause physical contact. A material is deposited when contact is made, regardless of the cause.

P 7- 6, L 15: Are particles charged either negatively or positively? If so, are there charges that reduce deposition as well as those that enhance it?

P 7- 7, L 10: By definition, if a particle is in the "inspired volume" it is inhalable. Conversely, if a particle is not inhalable, it won't be in the inspired volume. This sentence should read "—particle present in the ambient air".

P 7-9, L 1-13: For these citations, state whether the exposure is nasal, oral, or both. That makes a big difference for ultrafines, and the smaller the particle, the greater difference it makes.

P 7- 14, L 24 – P 7-15, L 3: You need to state that these are estimates from models, not actual measurements, and you also need to state the type of model used.

P 7-15, L 11-12: The sentence implies that there geographical areas where coarse PM are <u>not</u> present. Where would such an area be?

P 7-15, L 29: Again, do not use the word "aerosol" for "particle".

P 7- L 17: Once again, it's "particle" not "aerosol".

P 7-19, L 5: Give the geometric standard deviation for the ROFA.

P 7-19, L 18: Throughout the chapter, you should state whether the exposures were nasal, oral, or both. This is an important variable, and deposition really can't be understood without this information.

P 7- 22, L 3: This study measured total deposition, not "lung" deposition.

P 7- 22, L: It is not clear how a tumor would increase diffusion deposition.

P 7-24, L 13: It is not clear what the "shallow region of the lungs" would be. Would this be the

central airways?

P 7-25, L 14: Of course inhalability can be important for humans. It's important in a dust storm. It's important if you are riding a motorcycle (remember the old joke about bugs in the teeth).

P 7-25, L 25-26: What does "upper and lower airway bifurcations" mean?

P 7-26, L 6-7: Just say "—generation is constant" rather than "adopts a constant value". It's hard to see how an airway generation can adopt anything.

P 7- 26, L 14-20: A figure would help the reader understand what you are saying about deposition minima and maxima. A simple line graph showing fractional deposition with particle size for humans and rats, for example, would be useful.

P 7- 27, L 9: Mention whether or not these model predictions have been validated.

P 7- L 14: First, it's the MMAD of the particle size distribution, not the "aerosol" distribution. Second, give the geometric standard deviation of the size distribution.

P 7- 27, L 15: What does "comparable respiratory intensity levels" mean? I don't know what "intensity level" might imply.

P 7- 27, L 22: Again, has there been any validation? It is important throughout the chapter to indicate whether or not models have been validated against actual measurements.

P 7-28, L 9: The statement is incorrect. The study did not measure the "volume density of deposition", whatever that might be. The study measured, using a morphometric technique based on volume density, the <u>retained</u> material. A post hoc study of tissue cannot evaluate deposition, but only the amount and location of retained material.

P 7- 28, L 12-14: The statement is incorrect. It is not true that "different cells contact retained particles" in the two species. The difference was not absolute. There was relatively more material in the interstitium in one species and relatively more in the alveolar lumen in the other, but there was some material in both compartments in both species.

P 7- 28, L 21: The point is that there can be greater differences between abnormal humans and <u>normal</u> rats. The present wording doesn't convey this; it suggests that the greater difference you are talking about is between humans and rats.

P 7-28, L 23-27: This section inappropriately brings response into the dosimetric picture. Dose is dose regardless of response – these are related, but separate, issues. Interspecies dose extrapolation per se has nothing to do with interspecies differences in response or dose-response relationships. Comparative response has to do with both differences in both dose and response, but comparative dose has nothing to do with differences in response.

P 7.29, L 3: In summary, this section could greatly benefit from some tables or figures showing example results and comparisons. It also needs attention to which model predictions have been validated.

P 7-32, L 23-24: The magnitude of response also has to do with PM composition, not just with particle number.

P 7- 33, L 1-11: Lymphatics should be mentioned in this paragraph.

P 7- 33, L 14: Do you mean 5% by mass or number?

P 7- 33, L 17-18: Alveolar surface fluid is also transported, at least in some in part, up the airways. Surfactant of alveolar origin has been reported in the surface fluid of conducting airways. If this is true, then you should mention this path rather than implying that all PM-derived material solubilized in alveolar fluid is absorbed through the epithelium.

P 7-34, L 8: What do you mean by "nonuniform"? Do you mean spatially or temporally non-uniform within individuals, or are you referring to variability among individuals?

P 7- 35, L 5: You need to clarify throughout this chapter whether the statements about deposition site are derived from measurements or whether these are assumptions from deposition models. Most, if not all, are from the latter, which assume plug flows that are not likely to be absolute.

P 7-35, L 22: Deposition was "estimated", not "calculated". The latter term implies a certainty, or direct measurement, that doesn't exist here.

P 7-37, L 25-26: The phagocytic activity need not necessarily be decreased, it could be simply overwhelmed. More particles could reach the interstitium because of either or both effects.

P 7- 40, L 18: You need to explain what "mechanisms such as two-phase gas-liquid interaction" means.

P 7- 40, L 20: Do you mean that transport is <u>more</u> effective (ie, more rapid)?

P 7-41, L 13: It should read "—<u>those</u> obtained".

P 7- 41, L 21: I doubt this statement. I'd wager that more coughs occur in the U.S. annually because of internal reasons (viral infections, chronic bronchitis, etc.) than from an "inhaled stimulus".

P 7- 42, L 29: Again, there is confusion between deposition and retention. The 1 mg value is an amount of <u>retained</u> PM, not deposited PM. If you deposit that amount slowly enough, there will be no overload from the deposition.

P 7- 44, L 16: Do you really mean "random" here, or do you mean "uniform"? I think the latter would be a better term.

P 7-46, L 18: It should read "The model <u>results</u> were in good agreement", not that the "model" was in good agreement. "Models" don't agree with anything, but good ones produce "results" that do.

P 7- 47, L 7: Any results or validation here?

P 7- 47, L 15: Again, any validation?

P 7- 47, L 27: Once again, any validation?

P 7- 47, L 29: Please explain what "general dynamic equation for size evolution" is. I don't understand this, and there may be others like me.

P 7- 48, L 9-10: I think you are saying that the combined effects yield a narrower size distribution. If so, why not just say that, instead of saying "decrease the size nonuniformity" and "variance"?

P 7-50, L 16: It should read "—data are". Data is a plural word.

P 7-50, L 21: Define "acinar airways". That's a new term for this chapter.

P 7- 52, L 25: It should read "—rats and monkeys exposed—". The statement talks about two species, but you only name one.

Chapter 8: Toxicology of Particulate Matter

General Comments:

The chapter is a good draft, but needs considerable editorial clean-up of both text and tables, and some additional attention to content and conclusions. The former is addressed by numerous of the following specific comments. The latter pertains to the several places where sentences that portray conclusions (although not necessarily marked as such) that are unclear, misleading, or in conflict with one another. These are also addressed in the specific comments below.

The chapter could be better balanced in its treatment of the types of PM that are emphasized. As one example, it contains greater emphasis on ROFA than is warranted. Granted, there has been a tremendous investment in ROFA research, but aside from demonstrating the importance of soluble transition metals (which is important), the extension of this work to other ambient PM is limited. As one contrast, very little attention is given to "bioaerosols", and what information there is pertains almost solely to endotoxin. As another example, no convincing rationale is given for excluding the considerable database from engine emissions studies from this chapter. Diesel PM is cited for its potential adjuvant effects, but no mention is made of the several other potential effects of either diesel or other combustion PM and co-pollutants. Therein lies our greatest body of information on PM and co-pollutants, and some studies have explored the absolute and relative roles of different constituents of the mixture. It is especially astonishing that, while the emissions studies are ignored, studies of animals housed in urban and rural air, with no characterization of exposure, are cited. The latter have provided almost no useful information to date on the additive or interactive effects of PM and co-pollutants.

Regarding endotoxin, it is noted in one paragraph that ambient particles may have been contaminated by endotoxin – presumably during handling and storage. If this is a concern, and it may certainly be, why not note the concern more broadly with regard to many, if indeed not all,

of the studies using collected particles? This surely is not a concern only for those studies to which endotoxin effects are central.

The exposures cited in the text (and in some cases, in the tables) need to be more uniformly and more completely described. There are numerous instances in which studies are cited for which either the PM exposure concentration, time, or pattern are not given. Noting an effect, for example, of an exposure and only listing the concentration does not give the reader adequate information to place the findings in context.

The text and tables need to be screened to ensure that all abbreviations are defined. Some are apparently not defined.

The discussion of ultrafine particles seems to be ignorant of the portion of ambient ultrafine PM population that is in droplet, rather than solid, form. The discussion follows the classical ultrafine litany of greater penetration and surface per unit mass, but never mentions the ultrafine particles that are likely to spread, disperse, or dissolve after contact with liquid surface layers, and thus are probably never apparent to cells as "particles" per se. The points to be made are: 1) an acknowledgement that such PM exist, are ubiquitous, and need to be studied; and 2) there has been little or no research on this class of material.

Finally, the chapter does not do an adequate job of summarizing the key changes in our understanding of the toxicity between this and the last PM Criteria Document. The last section gets at this issue, but needs to be bolstered. As just one example, the Mechanisms of Action section (8.7.2) is a single paragraph that states that there may be more than one mechanism and that we don't know the mechanisms "unequivocally". While those are both true and understatements, there is not an indication of whether we know more about the plausbility of any mechanisms (ie, have more evidence) than we did last time. We do.

Specific Comments:

P 8-1, L 15: It should read "ambient PM", not "ambient air".

P 8-2, L 23: It is not clear what "total" means in "total exposure".

P 8-3, L 4-5: The distinction here is not clear. Presumably, both "low" and "high" toxicity PM cause effects because of size and composition. Are PM of low toxicity neither ambient or surrogate?

P 8-3, L 8-11: The selective treatment of diesel particles (DPM) is not clear and is of questionable logic. DPM can cause a range of non-cancer effects. They are an integral component of PM nearly everywhere, and can predominate in some microenvironments. The fact that EPA developed a separate hazard assessment for diesel emissions should not preclude the inclusion of DPM in this document. The selection of only the potential immunological effects of DPM for discussion in this document doesn't seem logical. At a minimum, this document should summarize the conclusions from the diesel hazard assessment.

P 8-3, L 14-16: There is something wrong with this sentence. First, it seems to mix the issues of inhalation and instillation. Second, it probably isn't true that most studies have used inhalation.

Probably more have used instillation. The points that 1) both methods have been used, and 2) most doses have been high, are valid, but the sentence is confusing.

P 8-4, L 5-14: This paragraph needs attention. First, the only study in healthy volunteers in Table 8-1 uses a concentration of 1000 : g/m^3, yet the text notes 2000 : g/m^3. Second, the text discusses clearance, but there is no report in the table about clearance. Third, if you are going to cite studies or results in the text that are not in the table, give the references.

P 8-4, L 17: If this is a 1997 reference, why isn't it in the table?

P 8-5, Table 8-1: First, give the exposure days/wk for the studies (first two) that use repeated exposures. Second, if the first study used only neutral sulfites, why is it in an "acid" table? Third, shouldn't the units in the Lee study be : g/m^3 and not mg/m^3?

P 8-6, L 9: How do you get "up to 6400" mg/m^3 if the exposures were for either 100 or 200 mg/m^3 for 45 min, as listed in Table 8-2?

P 8-6, L 22: References for the first statement?

P 8-6, L 25: Was it the vanadium or the responses that were elevated 9-fold? How do we know that the effects were due to vanadium in these subjects?

P 8-7, Table 8-2: For the Lay et al. Studies, why not give mass doses like the rest of the listings in the table? Did the paper not report mass doses (I think it did).

P 8-8, Table 8-2: In the last listing, was all of the ROFA vanadium pentoxide? Shouldn't the "particle" listing be ROFA?

P 8-9, L 13: It is not clear what a "host generated decrease in the availability –" means. Does this mean that reactive iron was removed after deposition?

P 8-11, Table 8-3: First, why list the concentrator type for the first study if you don't for the rest of the CAPS studies? Second, "CAPS" is not a sufficient descriptor. The location and time of concentration (at least something like "Boston, fall 1999") should be given. This document should avoid perpetuating the common, but naïve, notion that CAPS is some standardized or consistent material. Third, the age of the subjects is given for some studies and not others. If age is important (and it probably is), it should be given for all. The same for gender. Fourth, for the Kennedy et al. Study, give the dose administered. Fifth, what is the distinction between "instillation" in the Kodavanti et al. Study and "intratracheal instillation" in the Li et al. study? Finally, how could "instillation" in the Kodavanti et al. study be administered "6 hr/day – 2-3 days"?

P 8-13, Table 8-4: First, in the Brain et al. study, the time and location of sample collection should be in the "Particle" column, not the "Size" column. Second, the age and gender of the subjects should be listed. Third, where are "CFA, CMP, WC, and MCT" defined (Broeckaert et al. study, Costa & Dreher study)? Fourth, what does "emission source" mean in the Costa & Dreher study? What emission, what source? Fifth, in the Gardner et al. study, why note that the material was instilled in saline? Does this mean that none of the other studies used saline as the

vehicle if it wasn't listed? Are the "0.3 and 1.7" ml, mg, or what? Sixth, why is "exposure duration" listed as "N/A" for the Gavett et al. study. "Duration" is given for other instillation studies, and is presented as observation time after instillation. Seventh, no PM size is listed for the Hamada study. Eighth, what word is "alveotis" supposed to be in the description of the Kodavanti et al. 2000b study? Finally, were the deposited doses the same for instillation and inhalation in the Watkinson et al. study?

P 8-18, Table 8-5: First, give age and gender of subjects for each study. Second, in the Creutzenberg et al. study, does "retention increased" mean that clearance slowed, or simply that the lung burden increased? If that is the only reported effect, why bother to list the study?

P 8-19, L 1010: What were the lengths of the exposures cited in the paragraph. As a general principal, exposures need to be described by concentration, pattern, and length in order to be placed in context by the reader. Concentration alone isn't an adequate description of an exposure.

P 8-23, L 7: If by "injected" you mean instilled, then use "instilled" as is done elsewhere.

P 8-23, L 19: The important issue is not whether biologicals can "account" for the PM effects, the important issue is whether they might <u>contribute</u> to the effects. It's not a credible proposition that any single PM feature or type can "account" for the effects.

P 8-24, Table 8-6: First, if the PM concentration and size aren't known in the Cormier et al. study, and the only particle description is "swine building", what is the study doing in the table? We apparently have no idea what the exposure was or what part particles might have played in the effects. Second, in the Elder et al. study, does the 100 : g/m^3 refer to the carbon, the endotoxin, or both? Third, was there no estimate of PM concentration in the Rose et al. study? Overall, the poor characterization of exposures in the studies in this table renders most of them pretty useless for understanding the respiratory effects of bioaerosols. Aren't there any reports of effects of airborne pollen? Those are also bioaerosols.

P 8-26, Table 8-7: First, are "OTT" "MSH" defined somewhere? Second, why give the monocrotaline dose in the Costa & Dreher study – that isn't given for other monocrotaline references. Third, the location & time of collection of the CAPs should be given. Fourth, is "FOFA" something different than "ROFA"? Fourth, the gender & age of subjects should be given. Finally, the Minami et al. paper is a ridiculous citation. Both the experimental design and the interpretation are absurd. They injected undefined material into the jugular vein until the animals died, and noted that the heart acted up before death. You could do the same with tap water! This is an excellent example of the fact that not all published papers are worth including in this document. You can publish almost anything, but that doesn't mean that all publications contain meaningful information.

P 8-29, L 6: Here and elsewhere, the author's name is "Muggenburg", not "Muggenberg".

P 8-31, L 15-19: It is noted that there was little pulmonary effect in the dogs, but also that lavage neutrophils were doubled. That apparent conflict needs more explanation.

P 31, L 21: "Indice" should be "index".

P 8-31, L 26: "Suggests" should be "suggested".

P 8-31, L 26-28: This sentence doesn't make sense. Why do you call an increase in T-wave alternans an "anti-arrhythmic" effect?

P 8-32, L 6-19: This paragraph is confusing, and suggests that the author must be confused about these dog studies. It notes that Muggenberg (sic) found results in dogs exposed to ROFA that contrast with Godleski's results in dogs exposed to CAPs. That's an "apples and oranges" comparison. Later, it notes that the Muggenburg ROFA was collected at a different time than that used by Godleski, but never cites any Godleski ROFA study. What happened was the Godleski did studies with ROFA, then proceeded to work with CAPs. Muggenburg did studies with ROFA provided by Godleski, got different results than Godleski's ROFA results, and then found that the ROFA provided by Godleski wasn't the same as Godleski had used before. There isn't any connection between the ROFA studies and the CAPs studies. The point that the findings of little (Godleski) or no (Muggenburg) effect of ROFA suggests that the typically small amount of metals in CAPs may not be driving the effects of CAPs has some validity. In order to make that point, however, you need to clean up the paragraph.

The fact that different animal studies yielded different results doesn't reflect the problem of interspecies extrapolation, as stated. It reflects the difficulty of extrapolating among any differently-designed studies (animal or human). The animal studies quoted did not use the same exposure materials, and the results differed. That's understandable, but doesn't have much to do with interspecies extrapolation.

P 8-34, L 4-14: Another hypothesis that is not mentioned here is the direct transfer of PM from the lung to the heart. That has been shown to occur, although it's poorly documented and understood.

P 8-34, L 20: Has an effect of nutritional status on individual susceptibility to PM been demonstrated? If so, cite a reference. If not, don't imply that it has.

P 8-36, L 27-28: The difference in rat responses between the labs is more likely due to the difference in CAPs than to differences between rats or labs. This possibility is not even mentioned. As in other places, the wording here suggests the very naïve view that "CAPs is CAPs". You can hardly calibrate one response against another unless you show that the exposure material was identical.

P 8-37, L 7-8: I guess it depends on what you call a "limited number". There have been quite a few real-time exposures to CAPs now, and several to actual urban air.

P 8-37, L 15: I think you mean "no difference in lung volumes" rather than "no difference in lung volume measurements". The two are not the same.

P 8-38, L 20: "Organisms" should be "mice".

P 8-40, L 5: What kind of particles were acid coated?

P 8-40, L 15: The two "loci" should be "locus".

P 8-40, L 27: Why note that "replication of this study is necessary"? Why any more necessary for this particular study than for others?

P 8-42, L 13: Greater than additive to what, or in comparison to what?

P 8-43, L 18: This sentence says "daily exposure", but the preceding sentence says "single exposure". What kind of exposure are you really talking about?

P 8-45, L 14-15: How do the two quoted studies of BAL show that DPM cause an increased antigenic response in the nose?

P8-46, L 1: "Antimicrobial defenses against microbes" is redundant.

P 8- 46, L 16: What exposure level of DPM?

P 8-47, L 23-27: These two sentences are redundant.

P 8-48, L 10: There ought to be a paragraph in this section, perhaps here at the end, describing the different cell types used in the in vitro studies, and their relevance to cells in the human respiratory tract.

P 8-55, L 24-29: The point is made here that endotoxin might be a confounding factor in the response to ambient PM. It is good to note that endotoxin might be an important factor in some ambient PM. On the other hand, if there is concern that endotoxin contamination after the fact might have confounded this study, why would the same concern not be expressed for every other study that used collected and stored samples of not only ambient, but also other types of PM?

P 8-60, L 24: "Correlated" should be "correlate".

P8-62, L 3: Do you really mean a "combination of several components" as the sentence says, or do you mean a combination of metals? The subsequent sentence continues talking about multiple metals. "Components" includes both metals and lots of other constituents.

P 8-62, L 12-13: The statement suggests that all biological responses of ambient PM and ROFA depend on metals. Certainly, metals have been shown to play a key role in some responses, but you surely don't mean to imply that metals are the key to all biological responses to all PM.

P 8- 62, L 16-17: It should be "hours" and "sides".

P 8- 63, L 9-10: The last statement in the paragraph is correct, but the paragraph only deals with metals. The section is on reactive oxygen species. The material in the section tends to leave the reader with two false impressions: 1) that all reactive oxygen species are mediated by metals, and 2) all biological effects are due to metals, and by extension, to reactive oxygen species. Do you really intend to make these claims? If not, the paragraph ought to mention mediation of reactive oxygen species by other PM constituents, and make clear that you don't intend to imply that all biological effects are caused by this pathway.

P 8-70, L 23: "Time" should be "times".

P 8-71, L 5-7: There is evidence to support this statement for slowly-soluble, solid ultrafine particles, but that is only a part of the ultrafine PM population. This statement, like the entire section, seems to be ignorant of the existence of the portion of ultrafine PM that is not solid, but consists of droplets, mostly organic material and often condensed on nuclei of sulfur compounds. For example, this type of material makes up a sizable portion of the number count of ultrafine particles in engine emissions. To the extent that these particles are miscible in the liquid layer covering the epithelium, they would cease to exist as "particles" per se, and would not penetrate cells as such. While it is true that there has been almost no research on this class of PM, it is also true that we know it exists, and can't be ignored in the CD.

P 8-77, L 20-21: The type and ratios of pollutants are key factors that are missing from this recitation of factors affecting interactions.

P 8-78-79, Table 8-10: This table and the text seem to ignore the most common studies of combined PM-gas mixtures, studies of whole combustion emissions. Emissions studies are all studies of PM and co-pollutants, and several have tested the importance of different components. It is inappropriate to only cite studies of simple combinations of two or a few components and ignore studies of complex mixtures.

P 8-80, L 18: Again, what about the many emissions studies?. It is not true that the toxicology database is quite sparse in this regard.

P 8-81, L 9: "Interaction" should be "interactions".

P 8-82, L 16 to P 8-83, L 8: It is astonishing that these field studies of whole air (urban and otherwise) are cited as contributing to our understanding of the co-pollutant issue, while well-characterized combustion emission studies are not cited at all! These studies provide very little useful information. With regard to the topic of the section, they are basically ecological epidemiology studies with very few subjects of the wrong species. In line 26-27, it is stated that "extrapolation is hampered" by a lack of exposure characterization. What an understatement! Considering all the problems with these studies, it is questionable whether they merit inclusion at all. As in all air pollution studies, but especially true for studies of co-pollutant interactions, if you don't know the exposure, you don't know anything.

P 8-83, L 21-22: I disagree with this statement. The key to plausibility is not knowing the components and the individuals at risk. The key is to plausibility is understanding the linkage between the two (ie, a plausible mechanism).

P 8-85, L 13-14: This sentence contrasts with the earlier statement on page 8-63 that metals have been established as a key (it actually implied metals were the only key) contributor to health impacts of PM via reactive oxygen species. It is stated that the ROFA studies have important implications, but it doesn't state what the implications are.

P 8-86, L 5-14: This section on "bioaerosols" only talks about endotoxin. What about all the other bioaerosols? Endotoxin is seldom, if ever, actually a "bioaerosol". It is a contaminant of airborne PM. Pollen proteins, plant debris, and many other airborne materials of biological origin are not mentioned.

P 8-86, L 20: First, "PM is responsible" should be PM are the responsible". Second, there other health effects of concern for diesel PM in addition to the adjuvant effect. Why not mention them in this chapter?

8-87, L 29: It should say "animals with certain types of compromised health", or "animals with compromised cardiorespiratory health" or some such wording. Not all types of compromised health would be expected to affect susceptibility to inhaled PM (a broken toe, as an extreme, but illustrative example).

P 8-88, L 3-6: This closing statement needs work. First, validation of animal models is as important as identification, and this important point is overlooked in the section, and too often overlooked by researchers. Second, what is the connection between making "solid progress" and the fact that large numbers of people are needed for epidemiology studies? Would our progress be less solid if fewer numbers of people sufficed for epidemiologists? The author probably has a couple of good thoughts here, but it's not clear that they belong in the same sentence.

P 8-88, L 12-13: This sentence is trite. I think we can go beyond saying that there "may be" multiple mechanisms to state that research to date clearly indicates that there "are" multiple mechanisms.

Chapter 9 Integrative Synthesis

General Comments:

In general, the chapter is well-developed, and with some modest editing, will serve well as an integrated synthesis. With minor editing, it will hit approximately the right level of detail, and give appropriate attention to making the major points and drawing conclusions.

Some additional attention needs to be given to this chapter to accommodate the fact that many people will read only this chapter. It proposes to be a synthesis of all of the Criteria Document except the environmental effects. First, one wonders why the environmental effects couldn't also be summarized. Second, the chapter needs some additional definitions, attention to terminology, and figures in order to better serve as a stand-alone summary.

There are inaccuracies in this chapter that carry over from the same problems in preceding chapters. There are also sentences scattered throughout the chapter that don't make sense as written. This may have resulted from attempts to condense more expanded information in preceding chapters, but it needs to be corrected.

Specific comments:

P 9-3, L 14-15: While it is true that the term "aerosol" is often used incorrectly, why not use the correct terminology in the CD? "Aerosol" and "particle" are not the same thing. This chapter perpetuates the error.

P 9-4, L 16-18: It is stated that the nuclei mode is only distinguishable in remote areas or near sources. Elsewhere, it is stated that the nuclei mode is not observed in remote areas. Because

the nuclei mode is short-lived, it presumably would be found only near sources; thus, if it is in remote areas, there must be sources there. These facts need to be reconciled so the chapter presents a consistent story.

P 9-4, L 20-21: I have heard emission scientists distinguish "nanoparticles" as being in the 50 nm or less size range. Does the Agency care to set forth any criteria for these terms? That would be a useful service.

P 9-9, L 1 and 5: Wouldn't PM formed by condensation also be called "secondary"? That is, not all secondary PM is formed by "chemical reactions", right (or do you call condensation a chemical reaction)?

P 9-14, L 11-12: It is not clear if you are saying that these species exist, or should exist, or possibly exist, or what.

P 9-15, L 6: This statement conflicts with P 9-10, L 19-20 that states that nuclei mode particles are not found in rural areas. Let's settle on one story and stick to it.

P 9-15, L 28-29: The meaning of this sentence is not clear. The point about not being able to characterize particles because of lack of reference standards is not clear.

P 9-16, L 3: It should be "data ----<u>are</u> needed". Data is a plural word.

P 9-16, L 31: The point about particle-bound water is not clear. In fact, the whole issue of particle-bound water is not clear. Presumably, water is associated with some PM in the atmosphere. If so, then water is part of the particle, and you want to know the mass and number of particles, and their health effects, <u>with</u> water, not without. I can see how you would want to avoid data that include the accumulation of water by particles <u>after</u> collection, but why would you only want to know the mass of particles with <u>no</u> water?

P 9-18, L 1-2: It would provide useful perspective to give a typical portion of PM mass that cannot be speciated at present. It is often the majority of mass, not a tiny portion. That would be a surprise to most people.

P 9-20, L 3-4: State the time period of the children's health study, or the information here is not useful.

P 9-21, L 5-6: It is not clear what you mean by saying that the amplitude of the peaks is smaller than the daily means. That is not intuitive, and the reader (eg, me can't understand your statement.

P 9-24, L 4-5: It is not clear what you mean by "not influenced by exhaled breath" If exhaled breath actually influences the nature or concentration of materials in the breathing zone, then why would you exclude that effect? Another example of how you need a bit more explanation for this summary chapter.

P 9-26, L 8-24: This entire paragraph is difficult to follow. If the "attenuation factor" is worth mentioning (which I don't doubt), then you need to explain it and its application more clearly. It

can't be understood from this section alone.

P 9-27, L 10-14: This information is repetitive of earlier sections.

P 9-31, L 6: It should be "breathe", not "breath".

P 9-32, L 4: Is should be "alveolar", not "alveoli".

P 9-32, L 9-13: These sentences repeat errors that were noted in Chapter 8. First, the study did not evaluate deposition at all. It evaluated the location of retained material, and that could differ from the deposition site. Second, it is not true that different cells were exposed in the two species. The site of predominant retention differed between the species, but there was overlap. The same cells were exposed - just to a different degree, or with a different prevalence, in the two species.

P 9-34, L 22: Where are the data supporting this statement? I don't know of data showing that "overload" affects clearance differently in rats and humans. You would have to measure clearance rates in rats and humans having the same degree of "overload", and that hasn't been done.

P 9-36, L 12: What is a "biomedical" coherence? Do you mean "biological"?

P 9-37, L 3: Ambient PM exposure is always, not "usually", accompanied by exposure to other pollutants. Why be tenuous about this?

P 9-43, L 2-3: This sentence is not clear. What is the point about "identifiable" PM episodes?

P 9-60, L 26: This is the first time I've heard PM charged with affecting "morality"! I think you mean "mortality".

P 9-66, L 23-29: First, this 7-line sentence need broken up. Second, what is meant by "semi-individual"? Third, eliminate "studies" in line 26.

P 9-70, L 4: It should be "admissions of persons".

P 9-72, L 22: It should be "there are some data".

P 9-73, L 13-17: The sentence is confusing. It appears as though you are saying that CO could be a better surrogate for PM than PM itself. If that's not what you are saying, what are you saying?

P 9-75, L 15: "Suffers" should be "sufferers".

P 9-75, L 18-24: This paragraph is not clear. It is especially not clear what you mean by the sentence on lines 23 and 24.

P 9-76, L 11: It should be "these data were".

P 9-76, L 30: It should be "these data".

P 9-77, Figure 9-11: The label of the horizontal axis should be "Change in Peak Flow", not "pulmonary function". Peak flow is what was measured, and that's only one of myriad indices of pulmonary function.

P 9-81, L 1: It should be "relation to season".

P 9-82, Figure 9-13: First, in this summary chapter, you need to explain "posterior distribution". Second, there is no value in the inset box in the upper right hand corner of the figure because the numbers are all the same. What's the point?

P 9-83, L 14-15: If the advance is so noteworthy, it is worth explaining in this summary chapter. From this chapter, the reader doesn't know what a "distributed lag model" might be. The chapter explains lags, but not distributed lag models.

P 9-84, L 13: Again, what are "posterior mean effects"? When you first talk about the "posterior" terms on earlier pages, you need to explain what you mean.

P 9-84, L 23: What are "secular" components? Are they defined in this chapter?

P 9-85, L 2: Again, you need to explain the attenuation factor. This parameter and its significance are not adequately described in the chapter.

P 9-85, L 12-14: It is not clear what you mean by saying that correlations are not correlated. The sentence needs re-writing.

P 9-85, L 24: "Statical" should be "statistical".

P 9-86, L 15: It should be "correlations".

P 9-87, L 29: Use the term "48 contiguous states", as you do later.

P 9-88, L 6-26: It would help make your points if you included example figures from the Krewski et al. paper. Unless the reader is familiar with the figures, it is hard to envision the points you are making from them.

P 9-89, L 8-11: This sentence is not clear.

P 9-89, L 14: "Materials" should be "information".

P 9-94, L 8: You should just state that the material was ROFA, instead of "combustion particles". You talk about ROFA elsewhere, and using a different term implies that this was something different.

P 9-95, L 1: The statement is incorrect. It is clear that particles enter the blood. There is lots of evidence for that, unless you envision transport to other organs via some other mechanism.

What we don't know are the mechanisms and transport rates. We certainly know that transport occurs.

P 9-96, L 20-22: Perhaps this sentence was intended to start the next section. It doesn't belong where it is.

P 9-97, L 22: Gee, I thought the review draft diesel HAD was marked "do not cite or quote".

P 9-98, L 4-11: This section purports to refer to "bioaerosols", but like the bioaerosols section in Chapter *, it only refers to endotoxin. That's far too narrow a view of bioaerosols, and misleads a poorly-informed reader.

P 9- 98, L 13-20: The criticality of analyzing CAPs composition should be mentioned. Such studies place a premium on knowing composition, and are nearly useless without that information, yet CAPs studies often to not. This is an issue sufficiently important to mention.

P 9-98, L 22-31: It is not clear why this section is included under links between PM components and health. It is a related, but different subject, and warrants its own heading. In fact, it fits better under the next major heading.

P 9-101, L 26: Has "COH" been defined?

Paul J. Lioy, PhD

Chapter 3

Most of the information and analyses presented in Chapter 3 are typical of those presented in previous criteria documents on Particulate Matter (PM). Further, the analyses completed for the $PM_{2.5}$ concentrations collected with the new standard reference method are valuable as an initial assessment of annual or daily exceedences.

My major concerns are with the emissions and source apportionment sections. The focus of the emissions section is on sources of primary particulate matter. This is a good start, but is deficient with respect to sources of secondary particulate matter. The source apportionment assessment also provides more information on the nature of primary particle sources. At the same time the source apportionment analyses also point out the significant contributions of secondary particulate matter to the mass of $PM_{2.5}$, known as accumulate mode particles.

The source apportionment analyses can do an effective job investigating the percentage of contributions of secondary particles to the mass. They do not, however, provide quantitative information on the levels and types of precursor emissions which contribute to the formation of the mass.

In addition, there is no discussion on the chemistry that leads to the formation of secondary particles, and the residence time for fresh or aged secondary particles in the atmosphere. The only statement made that comes close to discussing secondary particles is on chapter 3, page 51. However, it states on line 26, that gaseous emissions "cannot be translated directly into

production rates for PM." Based upon the many years of particle formation modeling that has been completed by many laboratories, this statement is not accurate.

The lack of information or predictions for secondary particle formation is serious. This is based on the information presented in the current criteria document, and many papers published since 1976, which indicate that a large quantity of the mass of $PM_{2.5}$ in many urban suburban areas includes secondary particles.

The above deficiency requires that a section be added to the chapter that specifically addresses particle formation by photochemical smog or wintertime reducing smog processes. Modeling activities that include assessments of emissions inventories and a number of chemical processes, e.g., developed by Caltech, EOHSI, and other investigators, need to be described in the section. They are necessary to establish the types and levels of precursors that lead to the formation of secondary aerosol. The section could also provide a context for coupling the efforts for controlling ozone and other pollutants, to reducing formation and accumulation of particles.

Thus, I recommend that a section be added that focuses specifically on particle formation in photochemical smog by dark phase and sunlight phase processes. It should be developed to provide the proper context for evaluating the peak concentrations observed in the summertime. Condensation and heterogeneous chemical processes and aerosol production will assist in understanding wintertime chemistry. The section should also have a discussion on products, lifetimes, concentrations, and neutralization.

The new section will provide a framework for discussion about the significance of both "soot " and "secondary particles" in causing PM air pollution. It is essential that during the development of the SIP, we do not focus on sources that will provide marginal gains in particle control when it may be possible to benefit from ozone control strategies required to achieve the new 8-hour standard.

Some References:

Georgopoulos, P.G., Purushothaman, V., and Chiou, R. Comparative evaluation of methods for estimating potential human exposure to ozone: Photochemical modeling and ambient monitoring. J. Exp. Analy and Enviro. Epid., 7, 191-215, 1997.

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Georgopoulos, P.G., Walia, A., Roy, A., and Lioy, P.J. Integrated exposure and dose modeling and analysis system. 1. Formulation and testing of microenvironmental and pharmacokinetic components. Env. Science & Tech., 31, 17-27, 1997.

Georgopoulos, P.G. and Seinfeld, J.H. Nonlocal description of turbulent dispersion. Chem Eng. Sci., 44, 1995-2016, 1989.

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Korhonen, P., Kulmala, M., Laaksonen, A., Viisanen, Y., McGraw, R. and Seinfeld, J.H. Ternary nuclation of H_2SO_4, NH_3, H_2O in the atmosphere. J. Geoph. Res., 104, 26349-26353, 1999.

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Pilinis C. and Seinfeld, J.H. Continued development of a general equilibrium model for inorganic multicomponent atmospheric aerosols. Atmos. Environ., 21, 2453-2466, 1987.

Rao, S.T. and Sistla, G. Efficacy of nitrogen oxides and hydrocarbons emissions controls in ozone attainment strategies as predicted by the Urban Airshed Model. Water, Air, and Soil Pollution, 67, 95-116, 1993.

Roselle, S.J. and Schere, K.L. Modeled response of photochemical oxidants to systematic reductions in anthropogenic NO_x and VOC emissions. J. of Geo. Res., 100, 22929-22941, 1995.

Wexler, A.S., Lurmann, F.W. and Seinfeld, J.H. Modeling urban and regional aerosols: I. Model development. Atmos. Environ., 28, 531-546, 1994.

Chapter 5

General:

1. The chapter on exposures is a vast improvement over the previous version.

2. The chapter provides a reasonable summary of all recent studies on exposure, and interpretative analyses of previous work.

3. Unfortunately in the attempt to be current, the authors have forgotten to put some major concepts and results into a historical context. Some of the recent studies look as if they are presenting the first set of results on a particular issue. They clearly build upon previous

research. This should be acknowledged by referring to previous criteria document (AQCD, 1996) for further information on specific concepts.

4. There is still an over-emphasis on correlations. I have stated before, an "association (correlation) makes the poison" is not a valid concept. Every particle that deposits in the lung becomes part of a dose delivered to the individual. *Although the variability is very relevant to results obtained in many epidemiological studies that support PM health effects*, no one has yet shown that a constant or "quasi-constant" baseline level of PM from indoor or personal sources is irrelevant in causing health effects. This point is mentioned in the integration chapter (9), but not in chapter 5. The variable portion may provide the final stress to individuals who has had sustained contact and deposition of particles from all sources. So, both E_{ag} and E_{ig} may have partial influence on the ultimate dose affecting an individual at risk for one or more disease endpoints, especially potential acute effects.

5. The chapter needs another E descriptor, $E_{ov\text{-}rxn\text{-}iv}$ or $E_{(ioRn)}$. This is PM exposure derived from outdoor vapor (ov) reacting (rxn) with indoor vapors (iv). This is a source that could also vary with outdoor PM when the (ov) is ozone.

6. The range and distribution of many variables that affect PM penetration and deposition are nicely presented in the discussion. However, these are never integrated and placed into a final context for the uncertainties about the conclusions. The entire discussion is still attempting to steer us to a mean value for exposure used in epidemiological studies, a point that is well established. Unfortunately, the current approach ignores the distributional aspects of exposure to outdoor and other sources. It precludes further efforts in the staff paper to mention the uncertainties about the dose of specific agents or the entire mixture of PM from indoor and outdoor air, which could be relevant to acute or chronic outcomes. It precludes any discussion in the staff paper on the variety of exposures and sources, which may cause health effects. I do not believe the major ion contributing to the mean PM (e.g., SO_4^{-2}) is necessarily the chemical of concern. It may be an indicator, but we still need to define what it is an indicator of -- ambient $PM_{2.5}$ mass or toxic sub-fractions.

7. Last conclusion is a working hypothesis, but it is not the sole reason for understanding exposure. We need to eventually determine which dose or doses contribute to acute or chronic effects. The statement needs to be modified accordingly.

Detailed Comments:

P. 5.6, Table 5.1	Very good summary.
P. 5.7, Line 6	We have no definitive "outer limit" it is still a guess, and/or convenient location on the person. It is usually found somewhere within the personal envelop for inhalation.
P. 5.8, Line 21	Integral referenced to, NRC 1991. It was published previously by Lioy, 1990. Reference Lioy, P.J. "The Analysis of Total Human Exposure for Exposure Assessment: Multi-Discipline Science for Examining Human Contact with Contaminants" Environmental Science & Technology, 24, 938-945, 1990.

P. 5.11	Good summary of published activity pattern data.
P. 5.13 to 5.14, 5.3.2.2.2	Very simple explanation of mass balance model. Authors need to remind readers that all variables have ranges, and in some cases may change in value by a factor of 5 to 10. Therefore, sensitivity and uncertainty analysis are necessary when attempting to explain results.
5.3.2.3	The equation is a linear simplification of exposure and ignores possible synergisms. The authors need to provide qualifiers here!
5.3.2.3.1	Need to state that equilibrium is a simplification of indoor systems that are occupied by residents. Thus, equilibrium may only represent a "virtual" set of individuals or populations at potential risk. The alpha in Equation 5-9 can, and will, vary based upon lifestyle, meteorology, etc. Also, need qualifiers because of personal activities, housing characteristics, and particle size and composition.
P. 5.19	Very good introduction, and Table 5.4 is well done. There are others, but most are still work in progress (e.g., RIOPA study by Weisel et al; COPD by Koutrakis, et al.). Table 5.5 good summary table.
P. 5.30	Mage – Qualify to "<u>average person</u>" in PTEAM.
P. 5.31 to 5.35	The net result is that there are many different types of correlations and you can get many different results. Conclusion, we still need and more work on which variable(s) is (are) needed to represent personal ambient exposure. This is essential for assessing which compounds and which exposures cause the observed effects.
P. 5.37, Lines 9-10	A low correlation doesn't mean much, $r^2 < 0.05$!
P. 5.39, Lines 29-30	Is "tracked" the right term? This only explains 25% of variability.
P. 5.41	Subjects in Baltimore were very sedentary!! Could these individuals be described as stationary personal monitors?
P. 5.41	Sulfate is an indicator of ammonium sulfate, and not even the dominant acid species (sulfuric acid, ammonia bisulfate). In areas where there are large organic, or nitrate loadings, the SO_4^{-2} ion may not be an indicator of those portions of the mass. I think SO_4^{-2} is an indicator of the variability of aged secondary aerosol in the fine fraction.
P. 5.41, Lines 26-27	Confusing. SO_4^{-2} is a strong indicator of neutralized sulfur particulate exposure, where there are no indoor sources. In contrast, $PM_{2.5}$ has many sources besides SO_4^{-2}.

P. 5.43, Lines 6-8	Is this the appropriate way to interpret these data?
P. 5.43, Lines 21-29	Please eliminate, the section does not add anything to discussion.
P. 5.45	There is an assumption that there is no cross linkage between accumulation due to chemistry outdoors, and chemistry indoors. Ozone is present indoors and outdoors. Thus part of the PM assumed to penetrate indoor could be a mischaracterization of new particle accumulation indoors, due to reactions between ozone and VOC. The reason: ozone usually varies with $PM_{2.5}$, in the summertime.
P. 5.45, Lines 21-30	Agree with statement.
P. 5-47, Lines 1-10	However, the baseline PM from primary indoor PM sources may still account for the mass burden to the lung that is built upon by the variable portion caused by the outdoor concentration and exposure.
P. 5-48	These analyses are consistent with other previous studies. Need a reference to previous document, AQCD (1996).
P. 5-49, Line 10	Need to add the BaP data in THEES. Outdoor BaP was the same at all outdoor sites across 3 sampling periods. (See attached article by Waldman et al.). Is a good study of BaP indoor/outdoor/personal exposure. It indicates seasonal differences due to sources and activities.
P. 5-51 to 5-56	These are very good sections. However, the results are discounted or ignored when the authors try to construct mean linear relationships between E_{og}, and E_{ig}, etc.
P. 5-59	Indoor air chemistry is discounted and/or ignored. If we were to put it into an appropriate context for exposure there would be an $E_{ov\text{-}rxn\text{-}iv}$ or $E_{(ioRn)}$ exposure variable for particles generated by gases outdoors, reacting with gases indoors to produce fresh particles.
P. 5-61	Good section.
P. 5-61 to 5-63	Ignored in mass balance representations. The chapter authors lean toward averaging everything to point estimates. I would recommend sensitivity analyses to begin understanding and presenting a distribution of exposure.
P. 5-67	Lines 18-19 need to be at beginning of the paragraph.
P. 5-73	Need to add the BaP exposure results from THEES (see attached article, pg. 211-215). A very comprehensive analysis, which shows a lot about seasonal variability of indoor/outdoor sources and resultant changes in personal exposure to BaP.
P. 5-78	Oglesby et al 2000, lines 11-14 is a very good analysis, and is an honest

"qualitative" discussion about the uncertainties. But still ignores the fact that "association does not make the poison."

P. 5-79 (5.5.4) Ignores freshly generated aerosol indoors.

P. 5-80 (5.5.5) Good except for the lack of $E_{ov\text{-}rxn\text{-}iv}$ or $_{E(ioRn)}$.

P. 5-81 (5.6.1), Lines 8-15 Should bring to beginning of the chapter. All of page 81 is excellent, and should be moved closer to the front of the document.

P. 5-82, Lines 15-30 Need more research and not just hypotheses to explain "paradox". In the end, there may be complex synergisms, which preclude simple decoupling of indoor and outdoor particles. Again, this does not discount the strong epidemiological "association" established and summarized in volume 2. The comment tries to direct attention to the ultimate goal of the dose to the lung and other systems.

P. 5-82, Line 28 Add – Co-generation of fresh fine and ultra fine PM from outdoor air and indoor gaseous air pollutants.

P. 5-84, Lines 6-19 The E_{nonag} may not provide the variability, but will add to the daily baseline dose received by the lung.

P. 5-84, Lines 20-27 Good point, needs to be highlighted in conclusions.

P. 5-85 Need to include $E_{ov\text{-}rxn\text{-}iv}$.

P. 5-89 to 5-92 Good analysis of the problem. The uncertainties around the various mean values or at least the variability of each variable must be part of any presentation in the staff paper.

P. 5-90, Line 30, to 5-91, Line 1-3 Still does not discount the need to consider the presence and addition of the quasi-constant non-ambient mass. Exposures will yield a dose from indoor, outdoor, and personal PM.

P. 5-91, Lines 11-14 Good point, but lines 15-19 are just as important.

P. 5-93, Lines 21-25 Very important. Should be part of conclusions.

P. 5-95, Lines 5-7 It is a working hypothesis. Needs to be stated as such here and on page 101.

P. 5-95, Lines 29-31 Point about describing a single individual needs to be made earlier. The assumption in the text is that it represents the mean, and this has to be couched by a statement on distribution functions for all variables and the need to establish a probabilistic distribution of exposure, including

95%tile.

Missing – How will exposure data be used to address causality issues. A dose from indoor/outdoor/personal exposures to fine and coarse particles will be delivered to the lung. Do we need research that looks at the incremental toxicity of each for specific endpoints, or the synergisms that can occur among various toxic compounds of each fraction?

Mort Lippmann, PhD

CHAPTER 7

Page	Line(s)	Comments
7-1	12	after "aerodynamic" replace "a" with a "comma", and after "thermodynamic", insert ", and/or electrostatic".
7-1	15-22	change "translocated" to "clearance" and vice-versa. The usage of these terms is in error, and is inconsistent with usage later in the chapter.
7-3	1	insert "components of" before "aerosols".
7-3	14	delete "a", and insert an "s" after "parameter".
7-3	16	insert "from specific sources" after "aerosols". The ambient aerosol is generally composed of multiple log-normal distributions of aerosols from specific sources.
7-3	18	change "σg" to "σg".
7-3	19	change "(or 16th % particle size to the 50th % size" to "% particle size to the 50th % size, or the 50th % to the 16th % size"".
7-3	20	delete "aerosol", and insert "of a specific aerosol" after "sizes".
7-4	21	delete "cellular", and insert "cells of airway surfaces in the" before "ET".
7-5	11	change "1 :m" to "2 :m".
7-5	13	change ">0.5 :m" to ">1 :m".
7-5	19	change "lower" to "smaller" and delete "largest".
7-5	20	change ", which" to "that".

7-5	28	change "0.3 to 0.5" to "0.2 to 1.0".
7-6	4	insert ", but their length is the factor that determines interception deposition" after "length".
7-6	6	delete "when it is electrically neutral". This is an entirely redundant statement.
7-6	9	insert "generally" before "lose".
7-6	10	delete "slowly"
7-6	14	insert "positive and negative" before "charges".
7-6	15	change "some particles may result in an" to "particles will result in".
7-6	20	change "probably" to "often".
7-7	23	insert "ET" before "deposition".
7-7	30	change "0.3 to 0.5" to "0.2 to 1.0".
7-12	8	insert "that are either very large or very small" after "particles".
7-12	19-26	The data that are cited here should be described in greater detail and/or presented here in terms of a graph or table.
7-13	8	Reference should be made here to the work of Brody et al. (ARRD 123:670-699, 1981); Brody and Roe (ARRD 128:724-729, 1983); and Warheit et al. (Exp. Lung Res. 16:83-99, 1990) indicating that particles also deposit preferentially at bifurcations of alveolar ducts in small animals.
7-13	23	insert "distal to the larynx" after "volume".
7-14	16	insert "average" before "surface".
7-14	19	insert ", and furthermore do not take the concentration of deposition on carinal ridges into account" after "effects".
7-14	28	insert "The thoracic fraction of the" before "coarse".
7-15	3,5,6,14	change "NP" to "ET" for consistency with previous text in this chapter.
7-15	14	change "lungs" to "respiratory tract".

7-16	20	change "differ in" to "have different", and insert "distributions" after "parameter".
7-17	25	insert "large airway" after "increased".
7-28	9	change "deposition" to "retention".
7-28	12	insert "at the respiratory acini" after "tissue". The importance of the existence of respiratory bronchioles in humans, but not in rodents, should be discussed at this point.
7-28	30	insert "for specific surface regions" before "that".
7-34	4-5	The sentence is incomplete.
7-37	2	insert "toxicant" before "exposure".
7-44	21	This discussion is incomplete without a further elaboration of the fact that inhalation exposure results in concentrations of deposited particles on the bifurcations of both large and small airways.
7-52	31	This discussion is incomplete without a further reference to Nikola et al. (2000), which compared retention sites in lab animals (surficial) to humans (interstitial).
7-52	31	This chapter is incomplete without a summation indicating the most critical dosimetric unknowns and those amenable to resolution by further research.

CHAPTER 8

Page	Line(s)	Comments
8-3	13-14	The cited references refer to silica. Where can the reader go for an update on asbestos? The most recent ATSDR Toxicological Profile, or Lippmann (Environ. Toxicants, 2nd Edition, 2000) could be cited.
8-4	7,8	This sentence is redundant, and should be deleted.
8-6	4,5	This sentence is a real reach. The least that is needed here is a citation to the chapter section that attempts to justify this conclusion.
8-6	11-14	A reference citation should be provided to indicate where these data come from.

8-6	27	This discussion should be a separate paragraph.
8-6	31	Change "deposition" to "retention".
8-9	2	insert "is" before "present".
8-10	8	insert "some of" after "investigating", and "may" before "cause".
8-10	22-24	This sentence is far too definite a statement!
8-19	4-10	There should be a citation here to the later discussion of the "overload" issue in this chapter.
8-21	23	This discussion beginning here and extending to p. 8-23, line 11 provides strong evidence that transition metals may not be as important as repeatedly stated elsewhere in this chapter, and should signal a more general reassessment of many of the statements made elsewhere in this chapter.
8-25	19	insert ", but growing," before "number".
8-29	5	change "human" to "humans with".
8-29	26	change "health" to "healthy".
8-30	28	The statement ".... and that PM metal content was a better indicator than PM mass" is clearly not supported by the preceding discussion! There must have been more transition metal content in the ROFA than in the Ottawa ambient PM.
8-32	13,14	The preceding discussion of Godleski's research was restricted to concentrated ambient PM, not to ROFA.
8-62	10,11	The preceding discussion does not provide an adequate basis for such a firm conclusion.
8-62	13	change "subject" to "subjects".
8-62	17	change "side" to "sides".
8-65	29,30	How does the preceding discussion provide a basis for this conclusion? It could be made in any case without citing the preceding discussion.
8-67	5	If, in fact, the 94 mg/m3 was not an erroneous value, it is difficult to understand why such an outrageous and irrelevant exposure was worth citing in the CD.

8-70	23	change "time" to "times".
8-70	29	change "scrutinization" to "scrutiny".
8-72	29	change "to" to "that was".
8-73	7	insert "some of" before "the pulmonary".
8-73	8-10	If a contrast is to be drawn, then the concentrations at issue should be cited. If the work of Amdur and colleagues were included, the conclusion drawn would be quite different.
8-73	20-22	What does the 10,000 : g/m3 refer to? It clearly was not to acid. Was it to carbon?
8-75	1	What relevance can an exposure at 15,000 : g/m3 have to the discussion? Inclusion of citations to such ridiculous exposures do not belong in this CD.
8-75	10-13	What exactly are the authors saying here? Is there a serious intent here? If so, it should be justified and elaborated.
8-85	14	What implications? We, the readers, are at least entitled to some elaboration on what the implications in the authors' minds may be.
8-86	1	delete "However," insert "low concentrations of sulfuric acid on" before "ultrafine", and insert "metal oxide" before "particles".
8-86	2	change "focussed largely on" to "demonstrated"; change ". and" to "However,".
8-86	3	insert "also" before "have".
8-86	25	Add the following: "However, ambient diesel particle concentrations have decreased during the time of increasing asthma prevalence."
8-87	12	change "has" to "can have".
8-87	20	delete "however,".
8-88		Section 8.7 SUMMARY ignored the discussion in Section 8.5.3 on "Potential Cellular and Molecular Mechanisms" (pp. 8-58 through 8-68). Was it because it had no apparent relevance to the issues at hand?... or because the results cited were too various and confusing to show how further

research on biological mechanisms can be structured to advance the understandings needed to guide the identification of the physical and chemical properties of ambient PM that lead to adverse health effects. This summary section is incomplete without a reasoned summary of what previous research on biological mechanisms of PM health effects has determined, and how strategic planning for further research efforts can best be structured to resolve the unknowns in this important area.

CHAPTER 9
INTERACTIVE SYNTHESIS

General Comment

In general, this chapter is well organized and provides a clear summary statement and synthesis of the PM literature described in the preceding chapters. It will, of course, need some fine tuning, updating, and more definitive conclusions following receipt of CASAC and public comments. It is well on its way to serving its intended purpose and represents a welcome evolution from earlier PM criteria documents.

Specific Comments

Page(s)	Line(s)	Comments
9-3	3	insert "for regulatory purposes" after "pollutants".
9-4	4	change "enter" to "penetrate".
9-4	5	change "excluded" to "retained".
9-4	11	insert "or trimodal" after "bimodal" and "minimum between 1.0 and 3.0 ：m" to "minima at about 0.06 and 2.0 ：m". The figure referred to (Figure 9-1) is clearly trimodal, even though it represents the special case of near major roadways.
9-4	13	change "the" to "that".
9-7	10	insert "and PM10 includes only those coarse mode particles that can penetrate into the human thorax" after "equivalent".
9-7	28	insert ", which are predominantly in the fine mode" after "compounds", and insert ", which is predominantly in the coarse mode" after "material".
9-9	15	insert "relatively" after "only".
9-26	1	The authors should know better than to give credence to the notion of "some exposure analysts feel that ambient

		concentrations represent a surrogate for total personal exposure". This is a place where what we know should take precedence over ill-considered conjecture!
9-27	17	insert "source and/or" after "each".
9-27	27	change "several" to "many (~16)".
9-28	15	change "lower" to "smaller".
9-28	22	insert "directly proportional to the number of charges" before "inversely".
9-28	23	change "likely" to "generally".
9-30	5	change "and through segmental bronchi" to ", bronchi and bronchioles". There are "hot spots" on deposition on bifurcations at all branching levels, as I noted in my review of the Dosimetry chapter.
9-30	8-10	This statement is flat-out wrong, and needs to be reconsidered. Deposition peaks in the segmental bronchi.
9-32	29	"mucociliary" is misspelled.
9-33	24	change "(< 24 h)" to "(< 10 days)". The clearance via alveolar macrophages is minimal during the first 24 hours.
9-33	26	insert "moderately" before "soluble". Highly soluble materials do not retain their particulate form long enough to be translocated.
9-35	11	change "particles" to "deposits".
9-39	15	for consistency, insert "(SOx)" after "sulfur oxides", "(NOx)" after "nitrogen oxides", and "(O3)" after "ozone".
9-66	26	The "McConnell et al" reference is to one of the papers from the CARB sponsored children's health study at USC. The reference here should be to a paper by McDonnell et al on the AHSMOG data.
9-69		Figure 9-9 There is no translation given for the "HF" and "1 HD" caption designations in the figure. They refer to congestive heart failure and ischemic heart disease respectively. This also applies to Figure 6-6.
9-74		Figure 9-10 The hospital admissions data for Detroit reported by

			Lippmann et al. (2000) should be included in this summary presentation data. This also applies to Figure 6-7.
	9-79 and Section 9.6.2.3.3		This section is incomplete without discussion of a recent series of important papers from the Children's Health Study in Southern California. In particular, discussion needs to be added for the following:
	9-80		A. Papers that were cited in Chapter 6: 1) McConnell et al., EHP, 1999; 2) Peters, J.M. et al., Am. J. Resp. Crit. Care Med., 1999b and c; 3) Gauderman et al., Am. J. Resp. Crit. Care Med., 2000. B. Papers not previously cited: 1. Gilliland, F.D. et al. (2001). The effects of ambient air pollution on school absenteeism due to respiratory illnesses. Epidemiol. 12:45-54. 2. Avol, E.L. et al. (submitted). Respiratory effects of relocating to areas of differing air pollution levels. 3. McConnell et al. (in preparation). Childhood asthma exacerbation and fine particulate air pollution in Southern California. Contact Dr. John M. Peters at USC for copies of these papers.
	p. 9-90	11-17	The section on the ROFA studies needs to acknowledge that the effects observed were attributed to much higher concentrations than those that occur in ambient air.
	p. 9-104	1-4	This discussion needs to distinguish between infants and children. Premature mortality occurs among infants (< 1 year of age) but not in children over one year of age. Excess morbidity and functional decrements are seen in children, especially those active out-of-doors. Lumping the two groups together is misleading and incorrect.

CHAPTER 6 EPIDEMIOLOGY

General Comment

The authors of Chapter 6 are to be commended for an outstanding scholarly summary and synthesis of an enormous and highly complex literature on PM epidemiology. It comprehensively reviews the peer reviewed literature and systematically addresses what is known, what is uncertain, and what issues need to be resolved by further research.

One background topic not specifically addressed is the role that past regulatory decisions on the selection of PM indices have played in the evolution of the PM epidemiologic literature base. The adoption of PM10 in 1987, and of PM2.5 in 1997, have generated ambient air

concentration databases that made it possible for epidemiologic researchers to address and resolve many of the previously unresolved linkages between airborne PM and human health, and the newly authorized network of speciation samples holds promise for further advances in the near future on the identification of the more influential components of the ambient pollution mixture.

While there must, of necessity, be an end to the inclusion of newly accepted peer reviewed literature, the authors should make every attempt possible to include more of the emerging research findings as possible. In this regard, I call the attention of the authors to some of the potentially most important papers of which this reviewer is aware. In this regard, the text of this section should be expanded to reflect some recent relevant research reports, such as:

1. The report by Laden et al. on the follow-up study of the 6-cities cohort (Abstract ISEE-437, in: Epidemiol. 12(4): S81, July 2001), and the one by Pope et al. on the follow-up study of the ACS cohort (Abstract ISEE-205 in the same issue of Epidemiol.). The paper by Pope et al. (ISEE-205) describes a follow-up analysis of the American Cancer Society cohort in 51 U.S. cities for 16 years of mortality experience will report significant associations between PM2.5 and both cardiopulmonary and lung cancer mortality. (The Abstract that appears in Epidemiol., July 2001 does not describe the recently completed analyses.) There were no associations of mortality with the coarse thoracic mass (PM10-2.5).

2. The paper by Künzli et al. on the justification for relying on the cohort mortality studies for the best estimates of PM-related premature mortality (Am. J. Epidemiol. 153(11): 1050-1055, 2001).

3. Research reporting significant PM-related infant mortality to supplement the previous paper by Woodruff et al. (1997). These include an 8-city study (in the U.S.) by Kaiser, Künzli, and Schwartz (Am. J. Respir. Crit. Care Med. 163(5): 881, Apr. 2001) as well as 2001 ISEE Abstracts (Epidemiol. 12(4), July 2001). One, by Ha et al. (ISEE-134) describes PM10-related mortality in Seoul, Korea. Two others describe PM10-related reductions in birthweight, which provide coherence support for premature mortality. Bobak (ISEE-209) provides data for the Czech Republic, and Wojtyniak et al. (ISEE-331) provide data for Poland.

4. Research on the effect of PM on the health of children in Southern California beyond those reported in the PM CD draft. These include:

a. Gilliland, F.D. et al. (2001). The effects of ambient pollution on school absenteeism due to respiratory illnesses. Epidemiol. 12:45-54.

b. Avol, E.L. et al. (submitted). Respiratory effects of relocating to areas of differing air pollution levels.

c. McConnell et al. (in preparation). Childhood asthma exacerbation and fine particulate air pollution in Southern California.

Contact Dr. John M. Peters at USC for copies of these papers.

Specific Comments on Text

Preliminary draft comments of CASAC Particulate Matter Review Panel - Please do not quote or take out of context.

page	line(s)	Comments
6-4	12	add to end "while NO2 contributes to the formation of organic aerosols during photochemical transformations.
6-6	11	The generally accepted abbreviation for coefficient of haze is "CoH", not "COH".
6-7	7	insert "annual average" before "commmunity".
6-7	15	insert "short-term" before "mortality".
6-7	22	insert "than average" before "relative".
6-11	12	insert "Short-Term" before "Information".
6-39	1	change "most" to "nearly".
6-39	5	insert "are" before "generally", and change "comport" to "consistent".
6-80	14	insert the following sentence after "mortality". "On the other hand, the ACS cohort was largely Caucasian and above average in a socioeconomic sense, and its mortality RR would be expected to be lower than a more representative U.S. population".
6-83	1	delete "out".
6-105	7	change "newly" to "later".
6-108	26	change "constituent" to "index".
6-132	8	change "which" to "that" (also p. 6-184, line 26; 6-205, line 10).
6-138	7	change "which" to "that" (also p. 6-269, line 24).
6-140	18	change "is" to "are".
6-141	18	insert ", the variability of pollutant concentrations within the community," after "sites".
6-172	8	after "associations", insert the following words from line 9: "have been reported by several investigators".
6-172	31	insert "those" after "than".

1	6-175	15	transpose "U.S." and "various".
2			
3	6-175	19	delete either "Both" or "jointly".
4			
5	6-175	27	delete "Turning to non-U.S. studies". This study involved a mixture originating, at least in part, in the U.S., and it was based on the same kinds of measurements and models used in U.S. studies.
9			
10	6-180	13	insert "hospital" after "asthma".
11			
12	6-183	29	insert "in one second" after "volume" and change "FEV" to "FEV1".
14			
15	6-184	10	change "PF" to "PEF".
16			
17	6-184	16	change "PF" to "PEF".
18			
19	6-205	20	delete "As" and "other".
20			
21	6-218	3	change "that" to "which".
22			
23	6-225	28	insert "to be" before "expected".
24			
25	6-228	4	This section (6.4.2.3.) should not end without some interpretive statement and/or identification of what additional investigation is needed to make this alternative approach more useful for analyses of PM source impacts on human health.
29			
30	6-228	25	insert "cohort" before "study".
31			
32	6-229	11	insert "large" before "U.S.".
33			
34	6-230	12	transpose "as the exposure metric" with "a three-day running average".
36			
37	6-243	12	This section (6.4.4.) should not end without a discussion of which approaches might resolve this important issue.
39			
40	6-267	2,10	insert "thoracic" before "fraction".
41			
42	6-267	15	insert "well" before "beyond".
43			
44	6-268	20	insert "thoracic" before "fraction".
45			
46	6-268	28	change "may not yet be" to "are not yet".
47			

Preliminary draft comments of CASAC Particulate Matter Review Panel - Please do not quote or take out of context.

Jane Q. Koenig, PhD

Chapter 6

I complement the authors on an ambitious and generally successful job of summarizing recent studies in the field of epidemiology. I do have some major concerns.

Major

1) In my opinion, this chapter includes an unacceptable amount of editorial comment. It is my understanding that the purpose of the CD is to summarize the scientific literature and that comments and critiques of that literature are reserved for the Staff paper.
2) I know of at least two important papers that were not included in the document. This is of concern as there may also be others that I didn't notice. What was the process for inclusion of studies?
3) It is disturbing that the health effects of exposure to PM from wood smoke or other vegetative combustion sources are not mentioned. Wood smoke health effects should have been included in section 6.5. I believe this is a major oversight that should be corrected.
4) Apparently there is no discussion of potential associations between PM exposure and cancer. This may be an oversight.

Other general comments

Table 6-1 contains too much text. I think it detracts from the usefulness of the table (which is to provide an easily read comparison of data). This problem is present in the other large tables in the chapter as well. Would Table 6-1 be more useful if there were columns for lag times, RR, etc that are easy to scan? A table of significant associations between gaseous pollutants and mortality would be useful. I suggest notation of effects seen at concentrations below the current PM10 and proposed PM2.5 standards throughout the chapter.

5-1 2nd sentence, I think cardiac dysfunction should be mentioned right up front

5-45 Mar et al. gases were more highly correlated with PM2.5. PM2.5 and CO corr =0.85, with NO2 corr = 0.79 than noted in the CD

5-45 bad idea to use county for the unit. Certainly in King co people in gold Bar are not exposed to what Beacon Hill measures!! This is an example of using quick and easy to obtain data sets. Maricopa county appears to give very different outcomes than Phoenix.

5-46 -recommend that composition comments here be moved to 6.2.2.4

Table 6-16 This table would be more useful if the Emergency Dept studies were separated from Hospital Admissions. Also in general the tables in the Morbidity section are much easier to use than those in the Mortality sections.

Table 6-23 Respiratory Sx, lung function and biomarker effects.. What biomarkers are investigated? I didn't find any. Table 6-22 (asthmatic subjects) is entitled just Sx and lung

function.

6-216 6.4.1 This section appears to belong in ch 9??

5-225-227 Is it commonly accepted that SO2 cannot be a confounder for PM???

5-226 Discussion of the use of factor analysis is a good addition.

5-238 Mention of the Lipsett (1997) study is an opportunity to mention the role of wwod smoke as a constituent of PM. This should have been emphasized. In general there is not enough use of the role of geographical differences in PM composition as a means of understanding the toxic components.

5-246 Discussion of thresholds. If individual responses to PM prevent establishment of a threshold, how does that fit with the language of the CAA that requires setting a NAAQS for the most sensitive members of society??

5-266 6.5 Conclusions
2. Would it be more useful to describe heterogeneity as geographic differences in the composition of PM?

#3 I think short term v long term exposures need to be considered very, very carefully. We do not know to what extent prior exposure to air pollution is involved in the premature death cases in the short-term time series studies.

#4 The CF data may be telling us that there are geographic differences in PM

#5 This conclusion highlights effects during early pregnancy and post-natal periods. However these data are not presented forcefully in the prior text of the CD.

#9 As I mentioned earlier, I suggest a systematic description and summary of effects of co-pollutants.

#12 this paragraph (or a separate one) could include a discussion of the fact that there are likely different mechanisms for different PM-induced health effects. For instance, the mechanisms underlying air pollution aggravation of asthma will be entirely different from those underlying death from congestive heart failure.

#13 Should this paragraph be merged with # 4?

Comparison with the November 1999 draft CD

1) CASAC deemed that draft to be too encyclopedic and yet I don't see that the current draft is any less so.
2) CASAC recommended emphasis on cardiovascular effects and on infant mortality. I expected to see a separate table for these outcomes—certainly for infant mortality as there are only a few studies.
3) Is there really any more risk assessment in this draft than in the 1999 draft?
4) I believe that the strategy used to select the articles cited in the CD is still lacking in

spite of a specific request following the last meeting of CASAC.

Chapter 5. Human Exposure to PM and its Constituents

I am not by any means an expert in the filed of exposure assessment. That said here are my impressions on this chapter.

My overall impression of this chapter is that it is very different in scope from chapter 6 and 8. The emphasis appears to be a description of models available for describing exposure. As with chapter 6, this chapter would benefit greatly from a short paragraph at the beginning describing the goals and intent of the chapter. As with Ch 6 I am disturbed that the data on wood smoke have not be considered. The indoor/outdoor studies of fine PM from wood smoke may offer some useful information on penetration of PM indoors.

Another impression is that the chapter listed individual papers published since 1996 but did not compare and contrast these studies.

Specific comments

4-1 The second sentence should state that the lung AND HEART are the targets of concern.

4-4 Is the nomenclature μe accepted in the field. I don't like it—micro environments have nothing to due with scientific measures of micrometers etc.

4-46 In all figures the authors need to be very clear not are measured data and what are deduced from the models.

Should there be some description of exposure assessment to co-pollutants?

Roger McClellan, DVM

OVERALL COMMENTS

The present draft represents a significant step forward in summarizing the current status of knowledge on the health effects of ambient particulate matter (PM).

In my opinion, the document tends to overstate positive associations between increased levels of ambient PM and increased rates of mortality and morbidity and does not always convey the high degree of uncertainty in the date. While the NMMAP study represents a substantial advance in our identification of PM in some locales as having hazardous properties, the high degree of variability in effects estimates across the U.S. with lack of statistical significance in many cities suggests caution in interpreting relative risks of less than 1.1 and certainly for relative risks of less than 1.05. The use of normalized values of 50 : g/m^3 for PM_{10} and 25 : g/m^3 for $PM_{2.5}$ and $PM_{10-2.5}$ tend to exaggerate the actual findings. This could be illustrated by constructing a table presenting the actual estimated relative risk in percentage relative to the 10th to 90th percentile (or 25th to 75th percentile) range of the PM measurements.

The CD needs, in multiple places, to offer an admonishment that the quantitative statement of effects estimators, while useful for comparing and interpreting data, should not be used to make "body count" estimates or predictions for any city or region and certainly not for the U.S.

CHAPTER 6

EPIDEMIOLOGY – GENERAL COMMENTS

In general, this chapter provides a comprehensive survey of the epidemiological studies that have analyzed for PM associated health effects.

The chapter could be improved by development of an expanded introduction. Three key elements of an expanded version would be sections on (a) baseline health statistics, (b) the issue of inter-city and intra-city (temporal) variations in air quality and (c) statistical considerations. All three of these issues become critical to the conduct and interpretation of epidemiological studies. The baseline health statistics data are covered in a cursory manner in Chapter 9. That information should be presented at the beginning of Chapter 6 in an expanded format. To help the reader appreciate inter-city variability, a distribution histogram might be developed of the CVD/respiratory death rates for the 90 cities in the NMMAP's study. It would be preferable to show the rates for CVD and respiratory deaths separately. To illustrate intra-city temporal trends, the figure from Kelsall et al (1997) should be included.

For air quality data, distribution histograms could be developed for PM_{10} from the NMMAP's data to illustrate inter-city variability. The intra-city (temporal) trends could be illustrated using a figure from Kelsall et al (1997). The inclusion of these figures will help to illustrate the challenge faced in "teasing out" air pollution impacts from other impacts in the common diseases associated with PM.

The above discussion lays the general groundwork for the section on statistical considerations. In this reviewer's opinion, the most significant advances since the 1996 CD are derived from the NMMAP's study. This study benefited from the use of a common database and a common analytical methodology as well as increased statistical power related to analysis of data from 88 cities over a relatively long time period (1987 – 1994).

The chapter could be improved in balance with more attention given to issues of statistical certainty/uncertainty. The authors have tended to call attention to statistically significant results while tending to avoid calling attention to the lack of statistical significance in some studies.

CHAPTER 6

EPIDEMIOLOGY – SPECIFIC COMMENTS

Page 6-3, line 18: "Confounding and Effect Modification." This section addresses a very important point when it notes that "the health outcomes attributed to particles are not very specific." Indeed, the modifier very well could be dropped to make the statement more accurate. It would be helpful to the reader to illustrate the extent to which the majority of the typical health outcomes are attributable to other factors. Indeed, the terms – confounders and effects modifiers

– do not adequately relate the extent to which the health outcomes are attributable to factor others than the identified modifiers and effects modifiers.

Page 6-5, lines 28-30 and **page 6-6, lines 1-2**: It would be useful to add a paragraph or two here placing the pollutant increments in perspective. For example, for most of the U.S. increments of 50 ∶g/m^3 for PM_{10} or 25 ∶g/m^3 for $PM_{2.5}$ are not at all representative. The use of these increments tend to present an exaggerated view of PM effects.

Pages 6-6 and **6-7**: The approach used through the document of discussing the 1996 CD findings and then the post 1996 CD finding is confusing. I would prefer to see all of the evidence "weighed" to reach a current conclusion. The integrated finding could then be compared to the 1996 CD findings.

Table 6-1. The table should be expanded to include information on the effects estimation for pollutants other than PM when the individual study has evaluated other pollutants. Alternatively, this could be done in a separate table for those studies which have looked at multiple pollutants. In presenting the results, it would also be useful to complement information on pollutant effects estimators with information on actual pollutant levels so that the role of the individual pollutants would be more apparent.

Page 6-42, line 7 and **page 6-43, line 6**. It would be useful for the CD to include an expanded discussion of the handling of county-specific variables and co-pollutants in the NMMAP's studies. Specifically, it would be useful to include one or more tables that present specific data on the effects estimators used for other pollutants such as NO_2, O_3, SO_2, and CO and for temperature (both elevated and reduced). This would be helpful in understanding the total air pollution effect and the relative importance of PM. It is not sufficient (as in page 6-44, line 2-3) to relate that the PM_{10} effect on mortality "did not appear to be affected by other pollutants in the model."

In presenting the NMMAP's results it would be useful to include a graphical display that conveys the slope of the effects estimators for the 90 cities, or at a minimum, the regions plotted relative to the measured range of PM_{10} values used to derive the effects estimators. The latter values might be the 25th to 75th or 10th to 90th percentile of the PM_{10} values that were used in the analyses plotted on the horizontal and the mortality rate on the vertical.

Page 6-49, section 6.2.2.4 (The Role of Particulate Matter Components). This section should either begin with or end with a discussion of the challenge of characterizing the role of specific particulate matter components. Two major issues should be covered. First, epidemiological analyses can only be carried out on the components that have been measured. In that regard, a major problem relates to the past excessive domination of monitoring by concern for regulatory compliance, with a progression in the U.S. from TSP to PM_{10} and most recently to $PM_{2.5}$ measurements and with measurements of PM indicators made only every 6th day. The ability to test for the role of other components that may be significant will continue to be dependent upon having long-term measurements of these components. The second issue is the challenge of teasing out very small relative risks. It is apparent, and especially from the staff paper, that large study sizes are needed to obtain relatively stable and statistically significant results.

Page 6-58, lines 19-20: The statement indicating that wind-blown endotoxins and molds are contributing to PM10-2.5 fraction effects in the Phoenix area needs to be supported by references or omitted if it is mere speculation.

Page 6-58, line 2.7. In view of the role of SO_2 in the Wichmann, et al (2000) study, it would be appropriate to give an indication of the SO_2 levels measured and how they compare to levels measured in the eastern U.S.

Page 6-67, Source-Disputed Evaluation: It would be useful to review the analyses done by the NMMAP's investigators (perhaps even unpublished analyses) to determine if any of the results provide any insights into source-oriented impacts. For example, did the NMMAP's investigators explore any weekday versus weekend effects that might give insights into mobile source related effects?

Page 6-72, line 1: Show the Confidence Interval for excess other deaths; i.e., 1.3% increase per 50 : g/m^3 PM_{10}. It would also be appropriate to expand the discussion of other deaths to consider regional differences.

Page 6-73, lines 28-30: It would be useful to expand the discussion of sample size issues for sub-categories of disease. This could be done using the study size calculations in the staff paper for the NMMAP's study showing how the study size decreases progressing from total mortality to cardiac to respiratory causes. This discussion could be tied back to the base-line health statistics presented in Chapter 9 (tables 9-9 and 9-10).

Page 6-77, lines 23-26: The summary statement on biogenically-derived particles in the $PM_{10-2.5}$ fraction in this reviewer's opinion is over-stated relative to the evidence.

Page 6-80, lines 5-6: In view of the emphasis given to the relative risks for $PM_{2.5}$ derived from the ACS study, it would be useful to briefly review the methodology used in the ACS study to arrive at $PM_{2.5}$ values.

Pages 6-86 and **6-91** were missing from all copies of the CD provided to me.

Page 6-102, line 17 to **page 6-103, line 4**: It would be useful to give the low, medium, and high PM_{10} levels studied as an aid to relating the research to contemporary PM_{10} levels in the U.S.

Page 6-133, Individual-Level Studies of Cardiovascular Physiology. This section could be strengthened by including a discussion on the statistical problems of detecting small increases in "signals" for "low prevalence effects." This could be done by considering the study sizes needed to give statistically significant effects for cardio-respiratory mortality (per staff paper) and then applying these to the individual level studies, seeking to identify more subtle morbidity indicators.

Page 6-175, line 15 to page 6-176, line 17: In discussing the association of increased levels of PM and other pollutants with asthma, it would be useful to include information on the effects estimators for the other pollutants used in the various analyses. This will place the PM effects in perspective relative to other pollutants.

Page 6-177, line 27. This discussion needs to be expanded and integrated with data presented in tables 9-9 and 9-10.

Page 6-222, line 3: This would be an appropriate place to discuss the effects estimators for PM_{10}, O_3, NO_2, SO_2, and CO, provide an indication of typical levels, and discuss the relative contribution of each of the indicators to the total air pollution effect.

Page 6-245, Section 6.4.6, New Assessment of Threshold in Concentration-Response Relationships. The issues that should be discussed in this section go well beyond considering thresholds. This reviewer suggests the section be re-titled – "Concentration – Response Relationships for PM Indicators." The discussion should start with presentation of information on background levels of PM_{10} and $PM_{2.5}$, discussed elsewhere in the CD.

The discussion could then proceed to consideration of the range of PM indicator concentrations evaluated. This might include population-weighted data for some studies, such as the NMMAP's study. The section should include a summary statement concerning the calculation of population impacts of PM exposure. In my opinion, this would include a statement concerning the inclusion/exclusion of background levels of PM in calculating PM impacts for populations.

Page 6-258, line 29, Heterogenicity of Particulate Matter Effects Estimates: The section could be improved by providing additional baseline data, especially relative to the NMMAP's 90-city study. This could include inclusion of a table showing the average baseline rate (total mortality, cardiac and respiratory) for each of the cities studied, along with total population size. The baseline mortality for each cause might be shown for each city since this was the base against which changes associated with PM_{10} were evaluated. In presenting data on heterogenicity, it would be of interest to include data on cigarette smoking for each city and/or region, recognizing that cigarette smoking is the largest factor driving cardio-respiratory baseline rates.

Page 6-268, lines 3-6: This statement needs expanded discussion. If the effects estimates for PM_{10} hospital admissions are higher than the effects estimates (percentage-wise) for PM_{10} mortality, does that imply that PM is more effective (than other underlying risk factors) in causing hospital admissions as compared to mortality? If so, what is the potential explanation?

Page 6-269, line 3. Useful to add a sentence "However, the statistical association of health effects with PM acting alone or with other pollutants should not be taken as an indicator of a lack of effect of the other pollutants. Indeed, the effects of the other pollutants may even be greater than the effects attributed to PM."

Page 6-269, line 19: I suggest you omit reference to the APHEA study at this point in the document. While being a useful study it should not have nearly the same influence as the NMMAP's study in terms of relevance to the U.S. The quality of the aerometric data was much poorer than that used in the NMMAP's study.

Page 6-270, lines 4-7: This broad statement sounds intuitively appropriate. However, I suspect it is supported by very little data and the data were not reviewed in the CD.

Page 6A-2, Table 6A-1. For completeness, also present the data as rates; i.e., CVD deaths per 10^6/day. This will help in examining heterogenicity.

Page 6A-11: It would be useful in the interest of completeness to include the table shown as Appendix A, Table 4 in the Staff Paper in the CD.

CHAPTER 7

DOSIMETRY – GENERAL COMMENTS

This chapter is a useful summary of what is known concerning the dosimetry of inhaled particles. However, the chapter does not have as strong a linkage to the rest of the CD and to the issues of setting a NAAQS for PM as is needed. The chapter would be substantially improved by providing a better linkage to aerosols characterized with PM_{10} and $PM_{2.5}$ samplers at the beginning of the chapter. At the end of the chapter, it would be useful to have a section summarizing what can be predicted as the total deposition and regional deposition and retained burden for various exposure conditions likely encountered in the ambient environment.

DOSIMETRY – SPECIFIC COMMENTS

Page 7-2, line 28, 7.1.1 Size Characteristics of Inhaled Particles. This section needs to be expanded to provide a linkage to measurements of PM_{10} and $PM_{2.5}$. In its present form, this section is disconnected from the rest of the CD.

Page 7-4, Structure of the Respiratory Tract. This section would be enhanced by including one of the well-known figures illustrating the gross structure of the respiratory tract.

Page 7-9: The chapter would be enhanced by inclusion of a figure illustrating regional deposition in the human as a function of particle size.

Page 7-24: The chapter would be enhanced by including one or more figures illustrating inter-species patterns of total deposition and regional deposition for commonly used laboratory animal species and the species of interest, humans.

Page 7-38: The chapter would be enhanced by including one or more figures illustrating inter-species patterns of clearance and retained burden for commonly used laboratory animal species and humans.

CHAPTER 8

TOXICOLOGY – GENERAL COMMENTS

The introduction of the chapter could be strengthened with a better linkage to the epidemiology chapter. The epidemiology chapter relates findings from multiple studies showing an increase in health effects, primarily cardio-respiratory effects especially in susceptible populations associated with various PM indicators when assessed in larger populations (usually a study size of over 10,000 mortality or morbidity events times study days) with a relatively low prevalence

rate for the adverse events of concern. Restating this at the beginning of the Toxicology chapter will help provide a setting for consideration of the toxicological findings on PM in humans and laboratory animals under controlled exposure conditions. In my opinion, the toxicological findings have generally not been very informative, as to how PM may be pathogenic in humans or in identifying specific putative causative agents with PM. I suggest that the lack of progress relates to the blunt nature of current toxicological methods for tackling low probability of added effects when the diseases of concern have low prevalence rate outcomes even in susceptible populations.

It would also be useful if the introduction of the chapter could identify the challenge of moving beyond characterizing whether a specific material is hazardous; i.e., capable of causing adverse effects at any level of exposure to the critical issue of the relevance of the findings at typical ambient concentrations of PM.

The section of the chapter addressing susceptible populations should briefly consider the issue of cigarette smoking as a risk factor. I submit that the vast majority of increased health effects associated with PM in adult populations are observed in smokers or former smokers. These populations contribute a disproportionate number of individuals with cardio-respiratory disease and, thus, are the major susceptible population at risk from PM-related disease. It is noteworthy that to date a well-defined animal model has not been found for cigarette smoking induced cardio-respiratory disease. Smoking-related diseases develop slowly and are usually manifested late in life. The absence of such models is also reflected in the lack of well-developed and validated models of the common PM-related cardio-respiratory diseases. The minimal nature of respiratory disease in young rats exposed for months to heavy doses of cigarette smoke may also help rationalize the relatively refractory nature of rats exposed for modest lengths of time to PM and constituents.

The section of Chapter 8 on in vitro exposures lacks information that would help place the in vitro studies in perspective relative to in vivo exposures of humans to ambient PM. In comments on Chapter 7, I noted the need for calculations of deposition rates and steady state burdens of PM in humans exposed to various levels of ambient PM. Such information presented in detail in Chapter 7 could be summarized in Chapter 8 and provide a metric for comparison to the levels used in in vitro studies. A review of these in vitro studies suggests that the concentrations of PM and constituents studied are orders of magnitude in excess of any concentrations likely to be observed in humans at even the highest ambient concentrations encountered.

Chapter 8 also notes "there is growing toxicological evidence that diesel PM exacerbates the allergic response to inhaled antigens." (Summary statement pages 80-86, lines 17-180.) This statement and the supporting text needs to be qualified because of the high concentrations of diesel PM or extracts used. The last published EPA Health Assessment for Diesel Exhaust included a calculation of the quantity of diesel PM (and the organic fraction) inhaled and deposited. That calculation should be referenced in this document.

CHAPTER 9

INTEGRATIVE SUMMARY – GENERAL COMMENTS

This chapter represents an excellent start toward providing an authoritative summary of current

knowledge of PM. It could be improved with some signification additions.

Section 9.3 on ambient particulate matter could be enhanced by providing some summary data on past and current PM levels. This could include information from the latest EPA "Trends Report," the NMMAP's study on 90 cities and the temporal trend for PM (as TSP) and other pollutants for Philadelphia (from Kelsall et al, [1997]).

Section 9.4 on human exposures needs to be augmented with Figure 2-18 (Clayton, et al, 1993) from the Staff Paper.

Section 9.5 needs to be augmented with information on deposition rates and steady state levels for various regions of the respiratory tract normalized to typical ambient PM concentrations.

I suggest that a portion of Section 9.7 on Risk Factors be moved up after the present Section 9.5. This new section, entitled "Baseline Health Statistics" could help set the stage for the present Section 9.6 on Health Effects.

This new section should include the present tables 9-9 and 9-10 and additional information on key health statistics. I suggest this include summary baseline data on inter-city variability from the NMMAP's study for 90 cities. It should also illustrate temporal variability using the data for Philadelphia from Kelsall et al (1997).

At some point in the chapter it would be useful to include data, perhaps from the NMMAP's study on effects estimates for other key pollutants (O_3, NO_2, SO_2, and CO), to help provide perspective for the PM effects estimates.

Chapter 9 is seriously deficient in not providing a well-developed section on concentration-response relationships. This includes consideration of the threshold issue as well as the relationship between ambient concentration-response as natural background levels are approached.

Günter Oberdörster, PhD

Chapter 7 Dosimetry of Particulate Matter

Overall, this chapter summarizes well what has been presented in previous EPA documents and gives additional useful new information. However, there are several rather dogmatic statements which are unsupported and need either to be referenced or to be labelled as speculative. Some sections are also rather simplistic by stating the obvious, a bit more depth would help. This review summarizes on a page-by-page basis some suggestions for changes, deletions, additions.

Page 7-7, line 7: In addition to defining the term "inhalability" it would also be useful to define "respirability" since later on there appears to be some confusion as to which term should be used.

Page 7-9, line 2: CMD is not necessary, it implies a size distribution whereas here the upper limit is meant.

Line 4: The Frampton *et al*. study had both male and female subjects.

Line 9: Add after "diameter" the sentence: There was no gender difference.

Line 10: A statement could be added that this result compares favorably with the ICRP 1994 model.

Line 13: A sentence should be added here listing some of the values of the Jaques and Kim study, rather than giving the results only in relative terms.

Line 24: A sentence should be added here stating that at the same time, there is a shift in deposition sites from more peripheral to central or extrathoracic regions.

Page 7-11, lines 18-20: 94 - 99 percent is not consistent with the result reported in the previous paragraph (Yu *et al*.) where only 54% deposition was found for 1 nm particles, and these have the highest deposition efficiency.

Page 7-12, lines 7-11: The efficiency of the nose as a filter for ultrafine particles has to be seen in the context of the size within the ultrafine range. Whereas it can be very high for nanoparticles below 10 nm, the filtering capacity becomes less for ultrafine particles of 20 nm and greater.

Page 7-14, lines 10: Change "fine" to "ultrafine". In this paragraph again it would be helpful to give some of the values that were found by Kim and Jacques in their studies in terms of deposition efficiencies. A statement comparing their results with the ICRP model would also be helpful, for example, the total deposition in the alveolar region found by Kim and Jacques for 40 and 60 nm particles of ~33 and ~27 percent, respectively, are in excellent agreement with the ICRP model.

Line 30: To understand the modeling result it would be helpful to provide data on the size distribution of the environmental aerosols in terms of MMADs and geometric standard deviations.

Page 7-15, line 1: What kind of mathematical model was used? A brief descriptor would be helpful.

Lines 4-6: If 36 of the inhaled coarse particles were deposited in the lung, that doesn't add up if only 4 percent were in the tracheobronchial region and 2 percent in the alveolar region. Please check. Likewise, 9 percent of the fine particles deposited in the lung is not explained by 6 percent in the alveolar and a small fraction in the tracheobronchial region.

Lines 13-14: Here again 18 percent deposition in the lung is not explained by 2 percent in tracheobronchial and 3 percent in alveolar regions.

Line 23: I assume the cautionary note refers to the numbers (10^3, 10^5, *etc*.) but the general trend of differences between coarse and fine particle surface area and cell doses can also be derived from other models, *i.e*., ICRP, MPP Dep model.

Page 7-17, lines 24-26: I suggest to add here also that exercising will cause a shift in deposition sites from peripheral to more central airways as had been modeled by Martonen.

Page 7-18, lines 2: When differences in deposition between females and males are described here, these results as well as those from other studies comparing the gender-related deposition efficiencies should be critically evaluated: Both men and women breathed at the same tidal volume of 500 mL at 15 breaths/min, and this means for women, generally smaller than men, an increased minute ventilation compared to their normal breathing condition. Therefore, gender-related differences in deposition found here may be due to the fact that women breathed at a relative larger minute ventilation and would not show if both men and women would breath at their normal size-adjusted tidal volumes. A critical discussion along this line should be added.

Line 13: It would be helpful to add here a summarizing paragraph since the reviewed studies on gender differences show somewhat differing results and it would be

appropriate to have a summarizing concluding statement.

Page 7-20, lines 1-2: When comparing deposition efficiencies in the lungs of children *vs*. adults, it should also be considered that children have a higher minute ventilation per unit body weight compared to adults.

Line 26: Again, a summarizing paragraph would be helpful regarding age-related deposition differences.

Page 7-25, line 17: ">5 µm" should be "<5 µm" since it is this lower range where inhalability plays a role in deposition differences between rats and humans. Above 5 µm particle size inhalability is no issue for rats as far as the lower respiratory tract deposition is concerned. It would, however, be useful here to also discuss the importance of differences between rats and humans with respect to respirability of particles, since differences here are more pronounced: Particles >5 µm aerodynamic diameter are still well respirable in humans, but not in rats.

Page 7-26, lines 14-24: These model calculations by Hofmann and colleagues are not easily understandable. For example, the statement that alveolar deposition in humans was lower than in rats over the size range of 1 nm to 10 µm raises the question as to whether 10 µm particles at all will reach the alveolar region in the rat? This is clearly beyond the respirability range for rats. Did the model by Hofmann *et al*. consider the nasal filter in rats, or was it based on particles entering the trachea? This needs some clarification. In addition, when comparing deposition efficiencies between rats and humans, it should be mentioned here that to compare the deposited fraction alone is not enough: What one needs to also compare is the deposited amount per surface area which can give a quite different picture.

Page 7-27, line 8: Again, it is surprising that particle size-dependent deposition is qualitatively similar in rats and humans for particles up to 10 µm, see comment on respirability above.

Page 7-28, lines 3-14: This paragraph does not belong here, it is not dealing with deposition but with retention pattern after chronic exposure to particles in rats and non-human primates. In line 9 of this paragraph the term "deposition" should be replaced with "retention". The whole paragraph should be moved to a later section where retention is addressed.

Lines 15-22: In lines 19 and 22, differences between rats and humans are addressed without saying in which direction these differences go. This should be made clearer. Moreover, this paragraph is rather vague, it needs to be a summarizing paragraph to point out the major differences between rats and humans in a succinct way. The results by Hofmann *et al*. summarized above are not easy to understand, and they certainly require a concluding, clarifying summary.

Lines 23-31: This paragraph is a bit simplistic, and seems to have been written in a hurry. I suggest in line 25 to replace "dose response" with "retention". In line 27, how is the dose affected by species sensitivity? When different dosemetrics are addressed here in lines 28-31, then all of them should be mentioned, *i.e*., number of particles, surface area of particles (there are several studies showing the importance of particle surface area), the mass of particles as well as the volume of particles. The dosemetric in terms of particle number *vs*. mass, etc., depends also on the physico-chemical characteristic of the particle, *e.g*., for soluble particles the mass is probably still the more important parameter whereas any of the other parameters being more important for poorly soluble particles. It is also not clear what is meant in line 30 with the term "deposition": Is it deposition in terms of fractional deposition, deposition in terms of mass? The deposition density in the rat is not necessarily higher than in humans because of the smaller surface area of the rat lung, it depends very much on particle size and fractional deposition efficiencies as well as the ratio of rat to human lung surface areas. This paragraph needs to be

revised.

Page 7-29, lines 1 and 2: This concluding sentence stating that deposition density should be considered when extrapolating health effects seen in rodent studies to the human situation needs to be expanded in that other factors should be considered as well, such as dose in the specific region, dose per unit surface area, dose per cell (*e.g*., alveolar macrophage), and also particle parameters such as solubility, volume, surface area, size. Although deposition density is very important, other factors should not be neglected.

In this section on interspecies differences, it would also be useful to mention the availability of the Multiple Path Particle Deposition model (MPPDep) which allows the calculation of particle deposition in human and rat respiratory tracts assuming different exposure scenarios and breathing patterns and particle parameters.

In general, in this section on particle deposition efficiencies in the human respiratory tract and in the rat, a figure would be useful so the reader would not have to consult other publications for this purpose.

Page 7-31, Figure 7-3: If the size of the arrows in this figure indicates major *vs*. minor clearance pathways, then the arrow from phagocytosis by alveolar macrophages to passage through alveolar epithelium should clearly be a minor arrow since only a tiny fraction phagocytosed by macrophages takes this route (studies by Harmsen *et al*.), and the existence of this route might even be questioned. However, under particle overload conditions the translocation to interstitial sites *via* endocytosis by type I and type II alveolar cells becomes a major pathway, but this does not occur *via* particle-laden alveolar macrophages.

The meaning of the double-headed arrow from pulmonary capillary endothelium to phagocytosis by interstitial macrophages is not clear, does it mean that particles or interstitial macrophages with particles are coming back from the endothelium? Also, the arrow from phagocytosis by interstitial macrophages to pulmonary capillary endothelium is not clear: Is there compelling evidence that, indeed, interstitial macrophages with phagocytized particles are entering the pulmonary capillary endothelium?

Page 7-32, line 3: Not all solutes will be absorbed rapidly, it depends on the rate of dissolution from a particle as well as on the molecular size of the solute and other parameters to be discussed later.

Line 10: Probably meant here is that particles re-enter the airway lumen from mucosal sites, is there any reference for that?

Line 23 and 27: I don't think that the general statement can be made that the "magnitude of any increase in cell number (alveolar macrophages) is related to the number of deposited particles rather than to total deposition by weight". This would result in a huge increase in the case of deposition of ultrafine particles. Furthermore, cytotoxicity of a given particle is certainly a big stimulus for inflammatory cell increase, and if particles are soluble then the mass and not the number is the major determinant for eliciting cells. A better dosemetric to relate cellular responses to deposited poorly soluble particles would be particle surface area, and there are a number of studies which demonstrated that specifically for ultrafine and fine particles - given that they are not chemically different - particle surface area correlates very well with the increase in inflammatory cell numbers. Again, that applies only to poorly soluble particles and not for soluble ones where mass is the more appropriate dosemetric.

Page 7-32, line 31: This describes the pathway in Figure 7-3 of macrophages traversing the alveolar capillary endothelium directly entering the blood stream. Again, has this been demonstrated for macrophages with phagocytized particles?

Page 7-33, lines 1-11: There are a number of statements in this paragraph which need to

be supported by appropriate references. For example, what is the evidence for macrophages with phagocytized particles traveling to extrapulmonary organs? Are these new data? What is the evidence of particles binding to macromolecules?

Lines 17-29: The clearance of solutes is a bit superficially treated here, it is not that simple. It depends on the lipophilicity *vs*. hydrophilicity of solutes and the molecular weight. There are also different solubilities depending on the intra- *vs*. extra-cellular localization of particles due to respective changes in local pH. After dissolution or leaching of some components from a particle these can be binding of solutes (metals) to macromolecules; an important pathway also is transport *via caveolae* across the epithelium as well as the endothelium. The importance of differences between epithelial *vs*. endothelial pore sizes for lower molecular weight solutes could also be addressed here.

Page 7-38, line 1: Snipes and Clem used 3, 9, and 15 µm particles and found only the 3 µm to be translocated, did Takahashi really see 5 and 9 µm particles being translocated?

Lines 4-6: One has to be very careful when drawing conclusions with respect to lymphatic transport of particles based on intratracheal instillation studies: In such studies high doses are instilled as a bolus leading to local overload which messes up the normal clearance significantly and easily can result in lymphatic translocation which will not occur under normal conditions. Also the statement that particles >5 µm have significant deposition within the alveolar region is not correct for the rat. In the context of species differences related to lymphatic clearance, studies by Thomas *et al*. (1971) could be cited here showing differences between rodents and dogs, accumulation of particles in local lymph nodes being much greater in dogs.

Page 7-42, line 29: A most important feature of Morrow's hypothesis is that a volumetric overloading of alveolar macrophages occurs which eventually impairs its clearance function.

Page 7-43, line 11: I am not sure I understand why the slower alveolar macrophage-mediated clearance in humans compared to rats (it is always slower in humans) would cloud the overload relevance for humans: Humans also live about 25 times longer than rats.

Lines 14-15: It is hard to imagine how under normal environmental exposure conditions, overload will occur in compromised lungs. What compromised lungs would that be?

Line 26: Although it is generally assumed that intratracheal instillation delivers an "exact" dose to the lung, this does not mean that this dose is really found there shortly after the instillation because some of the material is rapidly cleared out by the following exhalations. The amount of this loss depends highly on the instilled volume as well as the instillation technique, *i.e*., synchronizing with respiration or not.

Page 7-44, line 9: It is not clear what is said here, the amount that is deposited in the lower airways by instillation can be adjusted, it is not due to by-passing the nose. Probably what is meant is that the distribution of material is different between the two techniques.

Page 7-45, line 11: It is unclear what is meant by percentage retention of particles: Is that the intercept of the retention curve with the ordinate, or is that the retention halftime? If the retention halftime is meant here that would be explainable since normally by instillation high doses are delivered which result in overloaded areas with retarded clearance. Thus, it might be better to compare inhalation and instillation-associated retention kinetics by describing the respective retention halftimes.

Line 18: The bulk of the instilled material certainly goes beyond the terminal bronchioles, otherwise you would see all of it being cleared in a short time by the mucociliary escalator. Of course, the very periphery of the lung is not well dosed, and as mentioned before, the coverage depends also on the instillation technique, *i.e*., synchronization with breathing or

not.

Line 29: Disposition of particles is only one factor determining their biological effects.

Page 7-50, line 1-6: For a discussion of "human equivalent concentration (HEC)" EPA's RfC document should also be quoted here. Furthermore, earlier in this section, emphasis was on the lung burden expressed as per unit lung surface area as being more appropriate, whereas here the amount per gram of lung is indicated. This might be confusing for the reader.

Lines 13-19: The Asgharian 2000 reference is missing in the reference list, is that a publication describing the MPPDep model which should be mentioned here as well?

As a general comment on this section, it should also be stated in a concluding summarizing paragraph that all models are just that: models. They have inherent uncertainties, which can be large and differences between model results can probably most of the time be explained by these uncertainties.

The title of this section is also somewhat misleading, both 7.6.1 and 7.6.2 deal with deposition and some clearance and retention, but the disposition of particles in terms of where particles move after deposition is not really addressed in this section on "Modeling of disposition". Much of what is reviewed in this section is already described in prior sections of this document and somewhat redundant.

Page 7-52, line 25-31: As we had discussed in the previous review, one has to be careful with the interpretation of the results by Nikula *et al*. (1997) since it was derived from a one timepoint post-exposure evaluation only: Rats with particle overload clear significant amounts to the regional lymph nodes, which means that the particles have to become interstitialized first; once in the interstitium, the rate of interstitial clearance to the lymph nodes may be much faster in rats than in primates which cannot be evaluated from a result obtained from one timepoint only. At this one timepoint, the interstitium in the rat could already be significantly cleared which would incorrectly be interpreted as less interstitialization. Therefore, whether this reflects truly a difference in retention pattern between rats and primates or a difference in interstitial clearance rate cannot be decided from the analysis at one timepoint.

Chapter 8

Page 8-1, lines 5-10: Among the questions listed here should also be the most important one, namely: Does PM at relevant ambient concentrations cause adverse effects?

Line 15: Change “air” to “PM”. Add at the end of the sentence in line 16: “or suspension”.

Page 8-6, lines 16-17: The study by Kuschner *et al*. used median concentrations of 133 mg/m^3, at which concentrations the particles are no longer ultrafines, so one has to be careful with their conclusion that there is no difference between fine and ultrafine particles. There is no question that chemical composition, surface radicals, *etc*., play a role as well, which is not disputed, just think about ultrafine PTFE *vs*. ultrafine TiO_2. But to exclude size as an important factor for toxicity is wrong. This comment has already been made by me for the previous criteria document and obviously was not considered.

Page 8-7 and 8-8, Studies by Osier: The inhaled concentration for the TiO_2 was 125 mg/m^3 for 2 hrs. (not µg) in order to match the intratracheally instilled dose in terms of pulmonary deposition.

Page 8-9, lines 19-22: The dose of 5 mg deposited in the human lung in this study is certainly much more than can be deposited from ambient air.

Page 8-10, line 18: Change "Teflon polymer" to "PTFE".

Lines 22-23: Again, the study by Kuschner *et al*. is cited here as demonstrating that composition and not particle size was responsible for health effects in this study. Given that the median concentration of the particles was 133 mg/m^3, these particles were no longer ultrafines, but aggregates. Obviously, in addition to size, composition is also a very important parameter and both need to be considered (see above).

Page 8-19, line 30: It would be useful to point out in this context that in general the intratracheally instillation studies failed to include a benign particle such as TiO_2 as a comparison to show that the effects observed are more than just a general particle effect.

Page 8-22, line 24: I strongly suggest to include the word "high" when the ROFA doses are addressed.

Page 8-23, line 30: The dose of LPS is given here as 5 or 50 µg. Is that the inhaled dose? Is that the dose in the nebulizer, or an estimated deposited dose in the lung?

Page 8-24, Study by Elder *et al*.: The concentration of 100 µg/m^3 is for the particles, not for LPS.

Page 8-30, lines 3-5: The effects observed here with ROFA inhalation should be viewed in the context that the inhaled concentration was 15 mg/m^3 and that inspite of this high concentration there were much lower or no effects compared to instilled ROFA which caused increased mortality.

Page 8-31, line 6: The concentrations of ROFA given were not only high, I suggest to describe them as "very high".

Line 19: Was the change in heart rate variability an increase rather than a decrease? I think what should be stated here is that the ratio of low and high frequency band of HRV decreased.

Page 8-32, lines 10-19: Here the two different dog studies by Godleski and Muggenberg are compared, however, the studies are significantly different from each other in that Godleski used CAPS and Muggenberg used ROFA, the particle size might also have been very different. Thus, it is difficult to compare the different findings between the two studies given also that storage of ROFA could have played an important role in altering its toxicity. It should also be considered that the dogs in the study by Godleski were exposed *via* a tracheostomy tube.

Page 8-34, line 4: I suggest to change "high concentrations" to "only high concentrations."

Page 8-37, lines 28-29: The exposure concentration of ROFA was 15 mg/m^3?

Page 8-38, line 17: Change "Teflon particles" to "ultrafine PTFE fumes".

Page 8-39, line 9: In this section of age-related differences in PM effects, the studies by Elder *et al*. should be included, they describe effects of inhaled carbonaceous model particles in LPS-sensitized rats of old and young age (Elder, A.C.P., Gelein, Finkelstein, J.N., Cox, C. and Oberdörster, G. Pulmonary inflammatory response to inhaled ultrafine particles is modified by age, ozone exposure, and bacterial toxin. *Inhalation Toxicology* **12** (Suppl. 4): 227-246, 2000; Elder, A.C.P., Gelein, R., Finkelstein, J.N., Cox, C. and Oberdörster, G. Endotoxin priming affects the lung response to ultrafine particles and ozone in young and old rats. Inhalation Toxicology 12 (Suppl.): 85-98, 2000).

Page 8-40, line 2: Is a fibrotic response an important endpoint for ambient PM?

Page 8-39 thru 8-45: In this section on genetic susceptibility to inhaled particles, a discussion on the dose levels used in the different types of studies would be useful to put them in perspective to ambient levels and deposited doses.

Page 8-48, lines 7-9: Among the severe limitations of *in vitro* studies are the dose levels which are generally orders of magnitude higher than experienced *in vivo*; and in addition the fact that only acute effects and mechanisms can be evaluated *in vitro* which could be very different

from mechanisms causing chronic effects *in vivo*. These significant limitations should be added onto the discussion in this section.

The title of **Chapter 8.5** refers only to *in vitro* exposures, which gives the impression that mechanisms can only be evaluated by doing *in vitro* studies. This is not correct, mechanisms are also evaluated by *in vivo* studies, in fact, the *in vivo* studies may be more important since they only can provide compelling evidence that any mechanistic pathway explored *in vitro*, indeed, is also operating under *in vivo* conditions which are obviously much more complex.

Page 8-57, lines 30-31: This two-line summary can be used for any type of particle and is not very specific, and it may be useful here to also again point out that the high doses that are used in these *in vitro* studies need to be considered. A sentence stating that detailed specific mechanisms related to ambient PM still need to be uncovered should be included here.

Page 8-65, line 8: What does the study of i.p. injection of ROFA contribute to an evaluation of mechanisms? This study doesn't seem to make much sense.

Lines 18-30: When comparing different dust materials in *in vitro* studies, it becomes very difficult to rank the toxicity of the different dusts because it is not known as to whether the different particles are internalized by the cells to the same degree, and also the dosemetric in terms of mass *vs*. particle number or size can significantly influence the result. The term "exposure–dose" used in line 30 is not clear, what does it mean?

Page 8-70, lines 15-16: This statement is only true if the chemical composition of the ultrafine particle and larger particle is the same, which should be added here.

Lines 15-29: Lines 27 – 29 provide an explanation for the observation that high doses of fine particles cause a greater effect than high doses of instilled ultrafine particles. Indeed, results of our earlier study (Oberdörster *et al*., 1992) demonstrated that the significant amount of ultrafine particles being interstitialized when high doses are instilled causes a decrease in the inflammatory cells in the alveolar space compared to inflammatory cell influx at lower doses of instilled ultrafine particles.

Line 31: The studies by Oberdörster *et al*. (2000), which are alluded to here, in old and young rats and mice used only ultrafine carbon particles, see also the publications by Elder *et al*. (2000, 2001) which were mentioned earlier in my comments.

Page 8-72, line 11: Replace "properties" with "area".

Page 8-73, lines 5-8: One has to be careful to characterize ambient PM as ROFA which has been used in a number of animal and *in vitro* studies. The ROFA that was used was collected from a bag house, and – as was pointed out earlier in this document – has a different metal content than the fly ash which is actually released into the environment, also metal solubilities are different. Furthermore, the high doses that were used in the ROFA studies need to be mentioned here as well.

Page 8-74, Section 8.5.5.2: This section reiterates studies that have been described before in this document. It should be remembered that the studies which are used here to demonstrate a specific mechanism to cause systemic effects have been run at very high doses or exposure concentrations, and thus, one needs to be very cautious to extrapolate these responses to relevant ambient concentrations of PM. What the studies do is show that the concept of a specific pathway or mechanism is valid in principle, but this needs to be validated and verified by additional studies using relevant exposures.

Page 8-81, line 26: Include (Elder *et al*., 2001).

Page 8-83, Section 8.7 Summary: This section provides a good summary of our present

state of knowledge. There should be a few clarifications:

Page 8-85, line 14: Implications for what? The implication I see here is to conduct further studies on the importance of metals, and that the ROFA studies have pointed out the importance of the metal concept for PM toxicity in general.

Page 8-87, line 16: Another ultrafine ambient PM concentrator was developed by Koutrakis and colleagues.

Section 8.7.1.2, Susceptibility: Among the susceptibility factors, not only genetically or induced compromised health should be listed but also age as a factor.

Robert Rowe, PhD

Below are my initial comments on the second draft CD and draft Staff Paper for the PM NAAQS. The EPA staff are to be commended for the work to date, especially recognizing the significant growth in literature relevant to the PM standard. My comments focus on economic and visibility perception portions of the materials provided.

Visibility Impairment Assessment

The Staff Paper Section 5.2.5, and a supplemental paper, address a proposed approach to address visibility impairment in terms of human judgement. While I encourage EPA to pursue this and other similar work, I believe more the identified plan may be insufficient, and the present work too preliminary (in terms of results, intended methods to make judgements, and how results will be used) to be presented as the potential basis for the secondary standard and given the attention it now receives in the Staff Paper. It is feasible that the results could suggest a SNAAQS at some locations that is more stringent than the health based NAAQS, at considerable cost to society. If that could occur, then the entire assessment must be much stronger than is presented as planned. Additional comments are below.

Little confidence should be attributed to one focus group of 9 people in one location (Washington, D.C), and this group should not be seen as sufficient to launch a multi-city assessment. I advise repeated groups in the first location to obtain more data and to address issues before proceeding to other locations, or to conclusions. Among the issues that could be considered are (1) how do the types and kinds of locations presented in the vistas alter the conclusions, if at all? (2) how much are perceived health concerns affecting the judgements, and how can this be better addressed? (3) what does it means when people say the impairment is acceptable or unacceptable? Does this mean every day or several days a year? Does this mean respondents are no longer impacted, or just that they think the likely perceived costs of further control may not be worth it (and on what basis do they make such a judgement), or that further improvements are not realistic. In this rating, respondents are participating in a stated preference (SP) assessment for which there is little of the typical SP set-up concerning the alternatives the respondents are evaluating. (4) Which measure will be used? For example, in the simple rating, the cross over point for unacceptable is 20 :g/m^3, but with the "how many hours a day" rating, 32.5 :g/m^3 is acceptable for as many as 4 hours a day by two-thirds of the respondents (and thus presumably a level of higher than 32 :g/m^3 for 4 hours a day would be acceptably on a simple 50% rule). (5) What will EPA do when there is no clear level at which most people shift from acceptable to unacceptable ratings (even at one location) – when there is a range of mixed opinion?

When moving to multiple locations, issues arise such as which vistas to present, what type of impairment (which varies in some locations), and how correlated will the ratings across locations be to existing conditions across locations (valuation literature would suggest status quo bias leading to anchoring and some adjustment to improved conditions).

While the approach follows similar work at the state and local level, it is not clear that the approach is sufficiently resolved for setting a SNAAQS. (1) What do you do if the "impairment" threshold is highly variable across different locations? Would EPA propose a variable SNAAQS by location? (2) What is an appropriate metric of impairment? Is it some level that is not exceeded on any day, or not exceeded more than a few days a year, or both? Is it haze, or brown clouds, or plumes, or all of these? (3) It may be beneficial to know how existing requirements (PSD, regional haze, or the primary NAAQS) would affect any potential visibility standards – what visibility levels would be meet and where might, if at all.
The economic valuation questions are preliminary, yet highlight there may be meaningful losses at visibility levels below the 50% rule for acceptable ratings. In the preliminary focus group the switch from 50% acceptable to 50% unacceptable occurs at 20 :g/m^3. However, when provided a choice, 5 of 9 would choose 15:g/m^3 and pay $50/year, as opposed to 22.5 :g/m^3 and paying $10/year (2 were indifferent between 15:g/m^3 and 22.5:g/m^3, and 2 chose 22.5:g/m^3 over the status quo of 32.5:g/m^3). This suggests a significant value for visibility conditions below the 50% rule level for either the simple ratings or hours per day ratings. I support further investigation into the economic valuation approach, with much more attention to survey design consistent with the stated preference valuation literature. To address the joint product issue between visibility and health, one might revisit the Carson et al. Cincinnati work performed for EPRI some years ago, which by the way showed losses down to just a few days a year of visibility impairment (e.g., an indistinguishable change when presented on an annual average basis).

There are important concerns with the proposed "focus group" approach to this assessment. Generally a study consisting of a group of focus groups across different locations may not be viewed as sufficiently rigorous for the intended policy application. More discussion should be held on this topic.

A few suggested editorial changes for the Staff paper (aside from continuing to include but reduce the discussion of this work). On page 5-16, I recommend active use and passive use values as opposed to use and non-use, to better identify that in some cases visibility is actively enjoyed, while in other cases it is passively enjoyed, and realize that it is often difficult to separate benefits by these categories (e.g., where does option value fall?). Page 5-23 of the staff paper was missing.

Criteria Document Chapter 4: Environmental Effects

General Notes Overall, this section is reasonably comprehensive. Two overriding considerations are (1) can the presentation be more focused to key questions in the setting of standards, rather than a litany of information and appendicies (this seems particularly true for the global climate sections), and (2) can economics, if it is to be addressed at all, be addressed more consistency in the various subsections.

<u>Section 4.2.2: Natural Ecosystems</u>

Lines 7 through 15. I recommend some terminology clean-up here, rather than propogating

terms inconsistent with the broader resource economics literature. All benefits from ecosystems can be described as ecosystem services. I think this could use revision, especially on page 4-20, to state something along the lines of "there are a wide range of ecosystem services, including (1) some with readily recognized market value (e.g., fish, timber, minerals,…) and (2) others services without current or readily identified market values. For the purposes of this discussion only, we refer to the first group as "market services" or "goods" and the second as "non-market services". Table 4.2 illustrates various market and non-market services provided by ecosystems…" Then, I think Table 4-6 is much more informative than Table 4-2 and could replace Table 4-2.

Page 4-83 identifies economic literature to demonstrate the significance of ecologic resources and services to mankind (Pimentel and Costanza). These numbers are presented, perhaps, with too much credence. There is significant controversy in the economics literature about the reliability of the specific estimates (See the Special Issue of Ecologic Economics, April 1998, and Freeman, 1999), not the least of which is that economics is much better suited to evaluate individual services, or better yet changes in service flows for an individual ecologic service, than it is to evaluate the total value of all ecologic services. Economics aside, most all agree that ecologic services are central to human life and obviously of substantial value. Consequently, substantive impact on ecologic services have the potential to have an important impact on human welfare.

Health Risk Assessment (Staff paper Chapter 4 and separate paper).

Staff paper 4-13, lines 10-26 discusses assumptions about changes in ambient conditions to meet standards, relying predominately on the rollback method. Using the rollback method is reasonable, but EPA should give careful attention to the proposed sensitivity analysis of alternative adjustments (lines 24-26). With increasing costs of compliance, episodic and other control strategies that reduce the highest concentrations may receive increased attention. Further, given that the population exposed is not uniform across concentration levels, and many concentration-response functions are non-linear, differences in the assumptions to reduce concentrations to achieve standards can have a significant impact on the risk assessment.

Deck et al, 2001 is cited several times, starting in the first paragraph, but is not available. It may be useful to provide this paper for this review.

Criteria Document Chapter 9

This chapter is well done and appropriately focuses on the larger questions of increasing consistency in the results of available literature and extensions to this literature. In terms of the important question of retaining or revising the existing $PM_{2.5}$ standard levels (15 ug/m3 annual average and 65 ug/m3 24 hours), little is presented in this chapter on the strength of the evidence, shapes of the estimated C-R functions around these levels, or effect thresholds (although this is touched on in Section 6.4.6).

Ronald H. White, M.S.T.

Chapter 6

General Comments

Overall, this chapter presents a comprehensive review of the extensive body of epidemiological studies published since completion of the 1996 particulate matter criteria document. The chapter properly interprets the studies discussed and appropriately emphasizes the strengths and weaknesses of the current scientific evidence of the health effects of particulate matter.

One key issue that requires further attention is the need for a consistent approach with explicit criteria throughout the chapter for the selection of the analyses from the studies included for summarization in the tables. For example, there are several criteria described (pg. 184; lines 8 –17) as providing the basis for selection of the analyses summarized in Table 6-19 and 6-20. However other summary tables do not explicitly provide the criteria for the selection of analyses summarized in the tables. Providing these criteria make the approaches used in selecting the analyses included for summarization in these tables and avoid concerns regarding author bias in the selection of analyses included for summarization.

Specific Comments

Pg. 6-226: This discussion regarding alternative methodological approaches to addressing confounding omits reference to the selection of study areas where potentially confounding air pollutant levels are relatively low (e.g. Vedal's 1998 study of asthmatic and nonasthmatic children in Port Albeni, B.C.).

Appendix 6A and 6B: There is no explanation in Chapter 6 as to the rationale for the inclusion of these appendices. While the recent studies regarding the relationship of heart rate variability to PM exposure provides one possible biological mechanism for the cardiac effects that may cause morbidity and ultimately premature mortality, other potential mechanisms for cardiovascular effects have also been identified (e.g. coagulation). Appendix 6B should be integrated into the body of Chapter 6.

Chapter 9
General Comments

While this chapter is somewhat improved compared to the previous draft in terms of writing style and providing some integration of information from different scientific disciplines, the underlying flawed approach of providing sequential summaries of what has already been summarized in previous chapters is retained. As such, this crucial chapter still does not provide the reader with a true integration of the key information identified in the previous chapters as being of major significance for the air quality standard-setting process.

In my December 1999 comments on the previous draft of this chapter, I had suggested an approach that would structure the information provided in this chapter as responses to several key questions regarding the health science information published since the previous Criteria Document. In his written comments on this current chapter, Dr. David Bates has also suggested a somewhat similar approach to structuring this chapter. As it currently is written, there is a significant amount of repetition of information already provided and summarized in the previous chapters. Key new information regarding PM exposure, toxicology, clinical studies and epidemiology are not currently integrated in a manner that informs the standard-setting process.

Specific Comments

Pg. 9-65; lines 2-5: The data audit performed for the HEI Reanalysis Project was not conducted by the study investigators as currently indicated in the text. The data audit was performed by an independent team selected by HEI to perform this function for the study.

Warren White, PhD

4.3 Effects on Visibility

First impressions

The visibility portions of the March 2001 draft CD were prematurely circulated for external review. Their inferiority relative to other parts of the document underscores the Agency's long-standing disdain for this subject. I can think of no harsher criticism of the material than simply reproducing a few of the highlights. Keep in mind that all come from fewer than two dozen pages!

Some of the lines could have been written by Edward Lear:

> "Light absorption by aggravated carbon at visible wavelengths is enhanced by no more than 30% and diminishes if encapsulated by a nonabsorbing aerosol." (P4-90, L 19)
>
> "At the surface, a variable fraction of the solar radiation is reflected back upwards, referred to as surface reflectance or the albedo, illuminating the atmosphere from above and below." (P 4-88, L 4)
>
> "The increase was largest in the summer and decreased in the winter." (P 4-108, L 28)
>
> "Some of the visibility impairment in northern California and Nevada, including Oregon, southern Idaho and western Wyoming, ..." (P 4-109, L 16)
>
> "Horvath (1993) reported that measured light absorption efficiencies for light absorbing carbon ranges from 3.8 to 17 m^2/g. According to Horvath (1993), calculated absorption efficiencies are too high, ranging from 8 to 12 m^2/g for monodispersed carbon particles." (P 4-90, L 12)
>
> "For most rural eastern sites, sulfates accounts for >60% of the annual average light extinction on the best days .." (P4-108, L 23)
>
> "However, several sites are not showing steady improvements in either visibility or $PM_{2.5}$, particularly in the number of worst visibility days (90^{th} percentile)." (P 4-111, L 20) [In other words, the number of days in a year is holding steady at about 365 per.]

There are tautologies and circular definitions of the sort associated with Lewis Carroll:

> "Human vision is one of the factors that affects the way an object is viewed." (P 4-86, L 10)
>
> "Discoloration may be used as a quantitative measurement of atmospheric color changes in

urban hazes." (P 4-98, L 2) [In much the same way as morbidity can be used as an indicator of impaired health.]

"The light-extinction coefficient is the quantitative measure of haziness, defined as σ_{ext} = K/visual range, where K is the Koschmieder constant. The value of K is determined both by the threshold sensitivity of the human eye and the initial contrast of the visible object against the horizon sky. The visual range may be calculated from the light-extinction coefficient using the Koschmieder equation .." (P 4-94, L 23)

There is simple technical ignorance:

"The cones, a receptor cell in the retina, govern visibility interpretations." (P 4-86, L12) [This is why an eyeball can be offended by haze even after surgical removal from the head. And why we see nothing after sundown.]

"Some of the light in the sight path is absorbed or scattered towards the observer. The remaining light is absorbed or scattered in other directions." (P4-86, L 24) [Leaving the observer searching in vain for any transmitted image.]

"The scattering and absorption efficiencies are determined by estimating the size distribution of each particle." (P 4-89, L 20)

".. the extinction coefficient that is calculated from the visual range, corrected to 60% relative humidity by the Koschmeider relationship." (P 4-109, L 29) [Versatile guy, that K.]

"Mie scattering is the scattering of all visible wavelengths equally (Shodor Education Foundation, Inc., 1996)." (P 4-87, L 1) [Which must be why Mie theory is computationally so trivial. Distressingly, this claim is supported by the citation, which turns out to be on-line training material developed for the Agency. The cited page also explains "how the shorter wavelengths which our eyes detect as blue when mixed, are scattered at a right angle. If the sun is directly overhead, the sun and sky look almost white while the sky is blue off to the
sides in the direction of the scattered light." The student might wish to step outside some clear day and check whether the horizon is indeed blue and the sky white.]

"The output of the Mie calculations includes efficiency factors for extinction, Q_{ext}, scattering, Q_{scat}, and absorption, Q_{abs}. The Q_{ext}, Q_{scat}, and Q_{abs} give the fraction of the incident radiation falling on a circle with the same diameter as the particle that is either scattered or absorbed. The light scattering or absorption efficiency factor (in units of m^2/g) is the change in the light scattering or absorption efficiencies per unit change in mass of the fine particle constituent. ... Multiplying the values of the light scattering efficiency factor by the aerosol volume concentration (in units of $\mu m^3/cm^3$) gives the value of the light-scattering coefficient, σ_{sp}, (in units of Mm^{-1}) for these particles." (P 4-89, L 15-26) [Students: find 3 different concepts of 'efficiency factor' in this paragraph. For extra credit, find 4 or more.]

".. over a 30-year period (1940 to 1990)." (P4-111, L 3)

There are misstatements of the Agency's own key regulatory concepts:

> "Visibility impairment is defined as any humanly perceptible change in visibility (light extinction, visual range, contrast, or coloration)." (P 4-85, L 3) [The hypothetical observer in a pure Rayleigh atmosphere thus experiences impaired visibility during each sunset and sunrise. Will the Sierra Club have to sue before the Agency addresses the long-standing and pervasive problem of twice-daily twilight?]
>
> "$dv = 10\ log_{10}\ (s_{ext}\ /10\ Mm^{-1})$" (P 4-95, L 13) [This makes one deciview correspond to a 26% rather than 10% change in extinction, and makes an extinction coefficient of 100 Mm^{-1} correspond to 10 dv rather than the 23 dv indicated in Figure 4-20. To be fair, this error is accurately reproduced from the 1996 CD, and is faithfully carried into the 2001 Staff Paper.]

Currency, competence, and relevance, by subsection

What are appropriate standards for review? In terms of currency and competence, a default option for the 2001 CD is to reprint the 6+ page summary of visibility effects from the 1996 CD, section 8.9.1. That text is clear and accurate. If new text is needed, it should be no less clear and accurate. In terms of relevance, I start from the presumption that any secondary standard for PM will be specified in terms of the health-based primary standard, currently $PM_{2.5}$ as defined by the FRM. A key burden of section 4.3, then, is to document a consistent relationship between visibility and measured fine particle mass.

4.3.1 **Introduction:** The second of the two paragraphs is up to date and appropriate (although the citation of the IWAQM document (USEPA 1995a) is puzzling). The first paragraph, in contrast, is confused and unnecessary – why should the 2001 CD open its visibility update with a garbled rehash of the Agency's 1979 distinction between reasonably attributable and regional haze?

4.3.2 **Factors affecting atmospheric visibility:** There is nothing in here drawn from work done since 1996, save for a passing reference to current visibility conditions from the Agency's latest trend report. Instead, there are odd definitions (e.g. "The visual range is the closest distance ..."), unused definitions (e.g. multiple scattering), incorrect definitions that were treated correctly in the 1996 CD (e.g. Mie scattering, as already noted), and a similarly varied range of 'facts'. It is dispiriting to find the Agency discarding a document that this Committee spent two years reviewing, in order to slap together an erratic new assemblage that is no more up-to-date.

Is visibility (as crudely indexed by, say, visual range) inversely related to ambient particle concentration (as crudely indexed by, say, $PM_{2.5}$)? One surely couldn't establish that point from this review! "Visibility impairment *may be* connected to air pollutant properties... Human vision is one of the factors ... the appearance of a distant object is determined by illumination of the sight path ... Visibility within a sight path longer than approximately 100 km .. is affected by changes in the properties of the atmosphere over the length of the sight path."

4.3.3 **Optical properties of particles:** Of the 23 different papers cited in this subsection, 17

were published by 1994 and 13 were reviewed in the 1996 CD. The technical discussion is very confused, and diverse extinction efficiencies are jumbled together with no context.

The Staff Paper includes a cross-plot (Figure 5-2) of ASOS airport visibility data versus 24-h $PM_{2.5}$ concentrations at Fresno, CA. This is exactly the sort of analysis that is needed to support a $PM_{2.5}$ standard for visibility and is missing from the CD. But it is only the first step: is the rest of the country just like Fresno? The CD instead gives us indigestible factoids: "Richards et al. (1991) reported a scattering efficiency for fine particles of ammonium sulfate of 1.2 m^2/g .. Sulfate scattering efficiencies have been reported to increase by a factor of two when the size distribution went from 0.15 to 0.5 µm .. The calculated scattering efficiencies for sulfates were 4.1 m^2/g for 100% mass removal and 3.4 and 5.6 m^2/g for 25% mass removal. Calculated scattering efficiencies for carbon particles ranged from 0.9 to 8.1 m^2/g .."

4.3.4 **Effect of relative humidity:** This section cites a higher proportion of recent work and is better written.

4.3.5 **Measures of visibility:** Of the 24 different papers cited in this subsection, 17 were published by 1994 and 13 were reviewed in the 1996 CD. I don't see any new information.

And including "fine particulate matter concentrations" as a "measure of visibility" is rather begging the whole question, is it not? The figure (4-22) supporting this subsection simply *assumes* a relationship for which the previous subsections laid no theoretical or empirical basis. (Note that the assumed Koschmieder coefficient in this figure differs from that used in the next (4-23).)

4.3.6 **Visibility monitoring methods and networks:** The new ASOS and expanded IMPROVE networks are appropriate topics for inclusion in this CD. The extinction budgets in Table 4-7 are problematic, however, because the text has given no theoretical or empirical basis for constructing and understanding them. It would better support a visibility-based secondary standard to summarize the measured extinction/$PM_{2.5}$ ratios and regression relationships observed at those sites with optical data.

4.3.7 **Visibility modeling:** Modeling can't be credible until the science is, so I didn't bother with this subsection.

4.3.8 **Trends in visibility impairment:** Much of this subsection (P 4-109, L 4-26) concerns extinction budgeting rather than trends in space and time. As noted above at subsection 4.3.6, the text has laid no basis for such apportionment. Moreover, some of the characterizations are a bit suspect -- for example, the statement "In several areas of the west, sulfates account for over 50% of the annual average aerosol extinction" is not supported by Table 4-7.

The trend discussion is largely carried over from the 1996 CD; Figure 4-23 is an update of Figure 6-112 by only three years and Figure 4-24 is a reprint of Figure 6-113.

Considering that this is supposed to be an incremental update of the 1996 CD, and that the data in Figure 4-24 end in 1992, it is hard to justify open-ended statements like "The haziness over the Gulf states increased between 1960 and 1970 and remained virtually unchanged since then."

4.3.9 **Economics of PM visibility effects:** Here, finally, is a subsection that does not just rehash and garble the corresponding 1996 account. Unfortunately, the new account seems inconsistent with the old, and the disagreement is nowhere acknowledged. According to the 2001 review (P 4-114, L 2), "The results indicate a willingness to pay per deciview improvement in visibility [in class I areas, capturing both use and nonuse recreational values] of between $5 and $17 per household." According to the 1996 review (Table 8-6), the willingness to pay per deciview improvement in urban visibility ranged from $8 to $231 per household (in older, more valuable dollars), with a median of about $100. If visibility is really worth that much more in cities than in National Parks, then why are almost all our visibility monitors in Parks? I couldn't find the $5 - $17 values in the cited reference, so I suspect that this is yet another instance of garbled reporting.

The bottom line for section 4.3 is that no coherent attempt is made to connect visibility with the health-based PM indicator.

A curious omission

The single most important visibility development since the 1996 CD has been the arrival of Regional Haze Rules. These Rules establish a framework for regulating visibility that any secondary PM standard will have to coexist with. Whereas any secondary standard will require scientific review by CASAC, the Regional Haze Rules already in effect were developed largely from an administrative/bookkeeping perspective. How does the Regional Haze bookkeeping square with the science reviewed by the CD? This is a question the draft studiously ignores.